No. 24-1936

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., and TEVA PHARMACEUTICALS USA, INC.,

Plaintiffs-Appellants,

v.

AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS LLC, and AMNEAL PHARMACEUTICALS INC.,

Defendants-Appellees.

Appeal from the U.S. District Court for the District of New Jersey
No. 23-cv-20964 (SRC), Judge Stanley R. Chesler

CORRECTED NON-CONFIDENTIAL JOINT APPENDIX

Daryl L. Wiesen
Christopher T. Holding
Louis L. Lobel
Jordan Bock
Thomas V. McTigue IV
GOODWIN PROCTER LLP
100 Northern Ave.
Boston, MA 02210
(617) 570-1000

William M. Jay
GOODWIN PROCTER LLP
1900 N Street, N.W.
Washington, DC 20036
(202) 346-4000

Natasha E. Daughtrey
GOODWIN PROCTER LLP
601 South Figueroa Street
Los Angeles, CA 90017
(213) 426-2642

Counsel for Plaintiffs-Appellants

Steven A. Maddox
PROCCOPIO
1901 L Street, N.W., Suite 620
Washington, D. C 20036
(202) 830-0707

Counsel for Defendants-Appellees

TABLE OF CONTENTS

Date	ECF No.	Title	Appx No.
	12-11	Answer – Exhibit K (Orange Book listing for ProAir® HFA)	Appx810-811
	12-12	Answer – Exhibit L (FTC Delisting Letter)	Appx813-816
	12-14	Answer – Exhibit N (Orange Book listing for QVAR 40)	Appx822-823
	12-15	Answer – Exhibit O (Orange Book listing for QVAR 80)	Appx825-826
	12-16	Answer – Exhibit P (Orange Book listing for QVAR Redihaler)	Appx828-829
	12-17	Answer – Exhibit Q (Orange Book listing for ProAir Digihaler)	Appx831-832
	12-18	Answer – Exhibit R (Orange Book listing for ProAir Respiclick)	Appx834-835
	12-19	Answer – Exhibit S (Orange Book listing for ArmonAir Respiclick)	Appx837-838
	12-20	Answer – Exhibit T (Orange Book listing for ArmorAir Digihaler)	Appx840-842
	12-21	Answer – Exhibit U (Orange Book listing for Airduo Digihaler)	Appx844-846
	12-22	Answer – Exhibit V (Orange Book listing for AirDuo Respiclick)	Appx848-850
	26	Declaration of L. Walsh in support of Teva's Motion to Dismiss – Exhibit 1 (Amneal's Notice of Paragraph IV Certification and Detailed Factual and Legal Basis of	Appx916-917, Appx921-952

Date	ECF No.	Title	Appx No.
		Non-Infringement, Unenforceability, and/or Invalidity) **(UNDER SEAL)**	
	26-3	Declaration of L. Walsh in support of Teva's Motion to Dismiss – Exhibit 3 (*Approved Drug Products with Therapeutic Equivalence Evaluations*, Food and Drug Administration (44th ed. 2024))	Appx974
	41-4	Declaration of R. Conroy in support of Defendants' Consolidated Brief – Exhibit 3 (Reed F. Beall & Aaron S. Kesselheim, *Tertiary Patenting on Drug-Device Combination Products in the United States*, 36(2) Nature Biotechnology 142-45 (Feb. 2018))	Appx1043-1046
	41-5	Declaration of R. Conroy in support of Defendants' Consolidated Brief – Exhibit 4 (Food and Drug Administration Guidance Document titled *Reviewed Guidance for Nebulizers, Metered Dose Inhalers, Spacers and Actuators* (Oct. 1993))	Appx1052
	41-9	Declaration of R. Conroy in support of Defendants' Consolidated Brief – Exhibit 8 (H.R. Rep. No. 116-47 (2019))	Appx1108-1169
	41-10	Declaration of R. Conroy in support of Defendants' Consolidated Brief – Exhibit 9 (Orange Book Transparency Act of 2020, Pub. L. No. 116-290, 134 Stat. 4889 (Jan. 5, 2021))	Appx1171-1175

Date	ECF No.	Title	Appx No.
02/20/2024	42	Consolidated Brief in Support of Defendants' Partial Rule 12(c) Motion and in Opposition to Plaintiffs' Motion to Dismiss	Appx1219, Appx1222-1224
03/22/2024	61	Federal Trade Commission's Motion for Leave to File Brief as Amicus Curiae	Appx1264-1273
03/22/2024	61-1	Federal Trade Commission's Brief as Amicus Curiae	Appx1274-1320
04/15/2024	65	Consolidated Brief in Opposition to Defendants' Partial Rule 12(c) Motion and Reply in Support of Motion to Dismiss	Appx1376
	65	Declaration of L. Walsh in support of Teva's Consolidated Brief – Exhibit 4 (Amneal Pharmaceuticals' Letter to the Honorable Elizabeth Warren and the Honorable Pramila Jayapal)	Appx1403-1404
	65	Declaration of L. Walsh in support of Teva's Consolidated Brief – Exhibit 6 (FDA's Jurisdictional Update: Metered Dose Inhalers, Spacers, and Other Accessories)	Appx1418-1420
	65	Declaration of L. Walsh in support of Teva's Consolidated Brief – Exhibit 7 (Drugs@FDA: FDA-Approved Drugs entry for ANDA No. 203760)	Appx1422-1423
	65	Declaration of L. Walsh in support of Teva's Consolidated Brief –	Appx1425-1426

Date	ECF No.	Title	Appx No.
		Exhibit 8 (Drugs@FDA: FDA-Approved Drugs entry for ANDA No. 209954)	
	65	Declaration of L. Walsh in support of Teva's Consolidated Brief – Exhibit 9 (FDA's Generic Drugs Program Monthly and Quarterly Activities Report)	Appx1428-1431
	65	Declaration of L. Walsh in support of Teva's Consolidated Brief – Exhibit 10 (Sunand Kannappan, *et al.*, *The Timing of 30-Month Stay Expirations and Generic Entry: A Cohort Study of First Generics*, 2013-2020, 14 CLIN TRANSL SCI. pp. 1917-1923 (2021))	Appx1436-1442
06/11/2024	92	Notice of Appeal to the Federal Circuit	Appx1534-1535
06/13/2024	112	Transcript of June 13, 2024 Hearing on Plaintiffs' Motion for a Stay	Appx1575
07/10/2024	111-1	Joint Claim Construction and Prehearing Statement	Appx1589-1591

Confidential Material Redacted Under Protective Order

Appendix Range	**Description of Redacted Material**
Appx916-917, Appx921-952	Declaration of L. Walsh in support of Teva's Motion to Dismiss – Exhibit 1 (Amneal's Notice of Paragraph IV Certification and Detailed Factual and Legal Basis of Non-Infringement, Unenforceability, and/or Invalidity)

The pages listed above contain material that has been excerpted from this appendix subject to the protective order entered by the district court. AppxI-XXIII. The confidential information in the excerpted pages relates to confidential information regarding Amneal's ANDA product.

FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., AND TEVA PHARMACEUTICALS USA, INC., Plaintiffs, v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS LLC, AND AMNEAL PHARMACEUTICALS INC. Defendants.	**Civil Action No. 23-20964 (SRC)** **OPINION & ORDER**

CHESLER, U.S.D.J.

This matter comes before the Court on two motions: 1) the motion to dismiss by Plaintiffs Teva Branded Pharmaceutical Products R&D, Inc., Norton (Waterford) Ltd., and Teva Pharmaceuticals USA, Inc. (collectively, "Teva"); and 2) the motion for partial judgment on the pleadings, pursuant to Federal Rule of Civil Procedure 12(c), by Defendants Amneal Pharmaceuticals Of New York, LLC, Amneal Ireland Limited, Amneal Pharmaceuticals LLC, and Amneal Pharmaceuticals Inc. (collectively, "Amneal.") For the reasons that follow, the motion to dismiss will be denied, and the motion for partial judgment on the pleadings will be granted.

This case arises out of a patent infringement dispute under the Hatch-Waxman Act between Teva and Amneal. Teva holds approved NDA No. 021457 for ProAir® HFA (albuterol sulfate) Inhalation Aerosol ("ProAir® HFA"), and owns certain patents listed in the Orange Book as covering this product: U.S. Patent Nos. 8,132,712 (the "'712 patent"), 9,463,289 (the "'289 patent"), 9,808,587 (the "'587 patent"), 10,561,808 (the "'808 patent"), and 11,395,889 (the "'889 patent") (collectively, the "Patents at issue" or the "Inhaler Patents"). Amneal has filed ANDA No. 211600, seeking to make and sell a generic version of ProAir® HFA. The following facts are undisputed. The Amneal ANDA contains a paragraph IV certification that the proposed product will not infringe any valid claim of the Patents at issue. After Amneal sent Teva the required notice letter, Teva filed the instant suit. The Amended Complaint asserts claims for patent infringement of the Patents at issue. Amneal filed an Amended Answer to the Amended Complaint asserting, *inter alia*, twelve counterclaim counts. Counterclaim Counts 1-5 seek declarations ordering Teva to delist the Patents at issue from the Orange Book. Counterclaim Counts 6-9 allege violations of the Sherman Act, and Count 10 alleges a violation of the New Jersey Antitrust Act, N.J.S.A. § 56:9. Counterclaims 11 and 12 are not at issue on these motions.

The Federal Trade Commission ("FTC") requested and was granted leave to file a brief as *amicus curiae*.

I. Teva's motion to dismiss Counterclaim Counts 6-10

Teva moves to dismiss Counterclaim Counts 1-10. The Court first considers the motion to dismiss the antitrust counterclaims, Counterclaim Counts 6-10. Teva contends that the

antitrust counterclaims are premised on two forms of alleged anticompetitive conduct: 1) improper Orange Book listing; and 2) sham litigation.

Teva contends that antitrust law provides no cause of action for improper Orange Book listing. First, Teva argues that because "Teva's patents are properly listed as a matter of law . . . any claim based on purported improper listing necessarily fails." (Pls.' MTD Br. at 25.) Later in this Opinion, this Court will consider and address Amneal's motion for judgment on the pleadings; as will be explained, the Court concludes that Teva's patents are *not* properly listed in the Orange Book as a matter of law. This conclusion does not support a Rule 12(b)(6) dismissal of an antitrust claim for improper Orange Book listing.

Second, Teva argues that, even if the Court were to find that the listings are improper, given the Trinko doctrine, "antitrust law does not create a cognizable claim for Amneal based on purported improper listing in any event." (Pls.' MTD Br. at 25.) In short, Teva argues that the instant case is analogous to Trinko, but this Court is not persuaded. The Supreme Court's syllabus for Trinko states the relevant key points of that case:

> The Telecommunications Act of 1996 imposes upon an incumbent local exchange carrier (LEC) the obligation to share its telephone network with competitors.
> . . .
> *Held:* Respondent's complaint alleging breach of an incumbent LEC's 1996 Act duty to share its network with competitors does not state a claim under § 2 of the Sherman Act.
> . . .
> (c) Traditional antitrust principles do not justify adding the present case to the few existing exceptions from the proposition that there is no duty to aid competitors.

Verizon Communs., Inc. v. Law Offices of Curtis V. Trinko, LLP, 540 U.S. 398, 398-99 (2004). Teva argues that the Listing Statute, 21 U.S.C. § 355, imposes upon an NDA holder an analogous obligation:

> [T]he Hatch-Waxman Act created a statutory obligation on a brand drug company to list patents in the Orange Book in order to help generic drug companies compete with the brand company by getting FDA approval for and launching their competing generic products more quickly. This duty is, for all relevant purposes, indistinguishable from the statutory duty imposed on incumbent service providers at issue in *Trinko*.

(Pls.' MTD Opening Br. at 28.)

Teva has failed to persuade this Court that the statutes at issue in the two cases are analogous. As the statement from the Supreme Court's Syllabus makes clear, the key attribute of the statutory provision at issue was that it "imposes . . . the obligation to share its telephone network with competitors." Trinko, 540 U.S. at 398. The Listing Statute does not impose any analogous obligation on the holder of an NDA. In fact, the Listing Statute says nothing about competitors or other drug companies; it speaks only about certain information that must be submitted "to the Secretary as part of the application." 21 U.S.C. § 355(b)(1)(A). That subsection, 21 U.S.C. § 355(b)(1)(A), lists eight subparagraphs which set forth what must be submitted to the Secretary as part of the application.

Teva offers nothing more than *ipse dixit* in support of its argument that the duty imposed by the Listing Statute is "indistinguishable" from the statutory duty at issue in Trinko. Teva's opening brief quotes the Supreme Court's discussion of the Hatch-Waxman Act in Caraco: "To facilitate the approval of generic drugs as soon as patents allow, the Hatch-Waxman Amendments and FDA regulations direct brand manufacturers to file information about their patents." Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S, 566 U.S. 399, 405 (2012). This says nothing about anyone helping competitors or cooperating with competitors. Teva has given this Court no basis to find that the Listing Statute imposes on NDA applicants a duty to aid competitors.

Furthermore, the FTC aptly summarizes the bases for distinguishing Trinko from the instant case as follows:

> *Trinko* is inapplicable because Amneal's counterclaims are not an expansion of antitrust law, the FDA does not directly police the Orange Book, and the statutory amendment to add a delisting counterclaim does not transform a patent enforcement framework into an antitrust regulatory scheme.

(FTC *Amicus* Br. at 33.) The FTC contends that the FDA's ministerial role[1] in Orange Book listings differs greatly from the extensive scheme for FCC regulation of telecommunications competition described in Trinko. The Telecommunications Act of 1996 established the regulatory scheme of interest in Trinko:

> The Telecommunications Act of 1996, Pub. L. 104-104, 110 Stat. 56, imposes certain duties upon incumbent local telephone companies in order to facilitate market entry by competitors, and establishes a complex regime for monitoring and enforcement. . .
>
> The 1996 Act sought to uproot the incumbent LECs' monopoly and to introduce competition in its place. Central to the scheme of the Act is the incumbent LEC's obligation under 47 U.S.C. § 251(c) to share its network with competitors.

Trinko, 540 U.S. at 401-2 (citations omitted). Teva does not contend that, in enacting the Orange Book listing provisions of the Hatch-Waxman Act, Congress sought to uproot any monopolies, nor that, as to the Orange Book, the FDA has any enforcement function. The only enforcement mechanism Teva points to is the delisting counterclaim – but this is plainly a judicial remedy[2] (as Teva admits), not an enforcement power entrusted to a regulator.

---

[1] See Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC, 60 F.4th 1373, 1378 (Fed. Cir. 2023) ("Notably, the FDA does not verify that submitted patents actually meet statutory listing criteria, nor does the FDA proactively remove improperly listed patents. *See Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1347 (Fed. Cir. 2003) ('[T]he FDA's . . . duties with respect to Orange Book listings are purely ministerial.')")

[2] In Trinko, the Supreme Court expressed skepticism that, where continuing supervision is needed, a court could serve as an effective enforcer. Id. at 415 ("An antitrust court is unlikely to

Compare this judicial remedy to the "regulatory structure" the Supreme Court described in Trinko:

> One factor of particular importance is the existence of a regulatory structure designed to deter and remedy anticompetitive harm. Where such a structure exists, the additional benefit to competition provided by antitrust enforcement will tend to be small, and it will be less plausible that the antitrust laws contemplate such additional scrutiny. Where, by contrast, there is nothing built into the regulatory scheme which performs the antitrust function, the benefits of antitrust are worth its sometimes considerable disadvantages. . . .
>
> The regulatory framework that exists in this case demonstrates how, in certain circumstances, regulation significantly diminishes the likelihood of major antitrust harm.

Id. at 412 (citations omitted). Teva has not demonstrated that the Orange Book listing provisions at issue comprise a regulatory structure designed to deter and remedy anticompetitive harm. In the absence of such a regulatory structure, the Supreme Court stated, it is more plausible that antitrust law provides additional scrutiny.

Having reviewed the enforcement mechanisms established by the Telecommunications Act of 1996, the Supreme Court concluded that "the [regulatory] regime was an effective steward of the antitrust function." Id. at 413. In the instant case, Teva does not even claim that there is any regulator with enforcement powers. This Court is not persuaded that availability of the judicial remedy of delisting significantly diminishes the likelihood of major antitrust harm, nor that this remedy alone is an effective steward of the antitrust function. As the FTC points out, the judicial delisting remedy does not provide for damages; that remedy alone cannot be an effective steward of the antitrust function.

---

be an effective day-to-day enforcer of these detailed sharing obligations.")

In sum, *amicus* FTC has persuasively distinguished Trinko. Teva has failed to persuade that Trinko is analogous and forecloses Amneal's antitrust counterclaims.

Teva argues as well that the plain language of the Listing Statute precludes an antitrust claim predicated on improper listing, citing 21 U.S.C. § 355(j)(5)(c)(ii)(II), which states:

> (ii) Counterclaim to infringement action.
>
> > (I) In general. If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) on the ground that the patent does not claim either—
> >
> > (aa) the drug for which the application was approved; or
> > (bb) an approved method of using the drug.
> >
> > (II) No independent cause of action. Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

Again, Teva presents only an *ipse dixit* conclusion about the meaning of 21 U.S.C. § 355(j)(5)(c)(ii)(II), without analysis or argument. On its face, subclause (II) delimits the authority of subclause (I), which authorizes the assertion of a counterclaim to correct Orange Book information in particular cases. The clear purpose of subclause (II) is to bar an independent suit seeking the relief stated in subsection (I) in the absence of a Hatch-Waxman infringement suit; it is designed to prevent the filing of claims for correction of the Orange Book as independent actions.

Amneal has asserted Counterclaim Counts 1-5, seeking orders of correction, and these appear to be permitted by 21 U.S.C. § 355(j)(5)(c)(ii); Teva does not argue that Counts 1-5 are not permitted by 21 U.S.C. § 355(j)(5)(c)(ii). Teva does not explain how 21 U.S.C. §

355(j)(5)(c)(ii) impacts the assertion of the Counterclaim Counts 6-10 under antitrust law. Counts 6-10 do not seek any order requiring the holder to correct or delete Orange Book information. Counts 6, 9, and 10 reference improper listing in the Orange Book as an example of an anticompetitive act. (Am. Answer at ¶¶ 281, 318, 322.) Count 7 does not mention the Orange Book. Count 8 references improper listing of patents in the Orange Book as an example of "a predatory scheme to monopolize the Relevant Market." (Am. Answer at ¶ 310.) Counterclaim Counts 6-10 do not seek correction or deletion of information in the Orange Book and do not fall within the ambit of 21 U.S.C. § 355(j)(5)(c)(ii)(I).

The Court finds that subsections (I) and (II) neither authorize nor prohibit Counterclaim Counts 6-10. Teva has offered nothing to support its contention that the plain language of these subsections prohibits the assertion of the antitrust counterclaims.

Teva next argues that Counterclaim Count 7, for sham litigation in violation of the Sherman Act, fails to state a valid claim. Teva's arguments for dismissal are all variants of the contention that Count 7 is unlikely to succeed at trial or summary judgment. As the Supreme Court stated in Twombly, "of course, a well-pleaded complaint may proceed even if it strikes a savvy judge that actual proof of those facts is improbable, and 'that a recovery is very remote and unlikely.'" Bell Atl. Corp. v. Twombly, 550 U.S. 544, 556 (2007) (quoting Scheuer v. Rhodes, 416 U.S. 232, 236 (1974).) Teva does no more here than argue that recovery on Count 7 is remote and unlikely; Plaintiff does not argue that Count 7 fails to plead a legally cognizable claim for relief.

Next, Teva argues that Count 6, alleging an anticompetitive scheme, fails to state a claim because the counterclaim components of that scheme all fail to state valid claims. Because this

Court has concluded that Amneal has pled viable claims for anticompetitive conduct, it is not persuaded that Count 6 is invalid because all the other counterclaims are also invalid.

The Court concludes that Teva has failed to persuade that any of the antitrust counterclaims fail to state a legally cognizable claim for relief, and the Rule 12(b)(6) motion to dismiss the antitrust counterclaims will be denied.

II. Counterclaim Counts 1-5 and the Listing Statute

As to the delisting counterclaims, Counts 1-5, Teva moves to dismiss them too. Amneal cross-moves for judgment on the pleadings on Counterclaim Counts 1-5. The Third Circuit has stated:

> We analyze a motion for judgment on the pleadings under Federal Rule of Civil Procedure Rule 12(c) under the same standards that apply to a Rule 12(b)(6) motion. Under Rule 12(c), a court must accept all of the allegations in the pleadings of the party against whom the motion is addressed as true and draw all reasonable inferences in favor of the non-moving party. A court may grant a Rule 12(c) motion if, on the basis of the pleadings, the movant is entitled to judgment as a matter of law. A plaintiff can survive a Rule 12(c) motion if her complaint contains sufficient factual matter to show that the claim is facially plausible, thus enabling the court to draw the reasonable inference that the defendant is liable for [the] misconduct alleged.

Bibbs v. Trans Union LLC, 43 F.4th 331, 339 (3d Cir. 2022) (citations omitted.)

In short, Teva contends that the delisting claims are premised on erroneous interpretations of the Listing Statute. As to Amneal's motion for judgment on the pleadings, Amneal and *amicus* the FTC argue that the listing of the Inhaler Patents in the Orange Book is improper and not authorized by the Listing Statute. Both of these motions turn on issues of interpretation of the Listing Statute.

The Listing Statute states, in relevant part:

(b) Filing application; contents.

> (1)
> (A) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application—
> . . .
> (viii) the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that—
> (I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or
> (II) claims a method of using such drug for which approval is sought or has been granted in the application.

21 U.S.C. § 355. Although the Orange Book is not mentioned by name in the statute, the parties agree that 21 U.S.C. § 355(b)(1)(A)(viii) states the fundamental requirements to effect the listing of a patent in the Orange Book. Subsection § 355(b)(1)(A)(viii) authorizes the listing of certain patents of three kinds: drug substance patents, drug product patents, and method of use patents. Teva contends that the Inhaler Patents are drug product patents, and that they are properly listed pursuant to § 355(b)(1)(A)(viii)(I).

Subsection § 355(b)(1)(A)(viii)(I) states two requirements: 1) the patent must "claim[] the drug for which the applicant submitted the application;" and 2) the patent must be directed to a drug substance or a drug product. This Court finds that the listing issue in this case turns on the interpretation of the first element and concludes, in short, that the Inhaler Patents do not claim the drug for which the applicant submitted the application.

There is no dispute that the Inhaler Patents contain no claim for the active ingredient at issue, albuterol sulfate. Amneal contends that the Inhaler Patents do not meet the requirement that they claim the relevant drug. The FTC agrees.

Teva points out that the word "drug" in § 355 is expressly defined in 21 U.S.C. § 321(g)(1):

> The term "drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).

The Court acknowledges that this definition includes articles intended for use in the treatment of disease, and that the ProAir® HFA inhaler falls within its scope. The problem for Teva is that this broad statutory definition of drug does not suffice to establish that the Inhaler Patents claim the drug for which Teva submitted its application, NDA No. 021457.[3] Teva offers the FDA approval letter for this NDA, dated October 29, 2004; the first line of this letter states: "Please refer to your new drug application (NDA) dated January 30, 2003, received January 31, 2003, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for albuterol sulfate HFA Inhalation Aerosol." (Answer Ex. A at 1.) According to the FDA, the drug for which the applicant submitted the NDA is "albuterol sulfate HFA Inhalation Aerosol."

Furthermore, the Amended Complaint states:

> 45. Teva Branded is the holder of New Drug Application ("NDA") No. 021457, under which FDA approved the commercial marketing of ProAir® HFA (albuterol sulfate) Inhalation Aerosol on October 29, 2004. ProAir® HFA (albuterol sulfate) Inhalation Aerosol is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive

[3] It is not sufficient that a patent claim a drug that falls within the scope of the definition of "drug" in 21 U.S.C. § 321(g)(1); the statute requires that the patent claim ***the*** drug for which the applicant submitted ***the*** application. Teva overlooks the significance of the statutory language that modifies the phrase, "the drug."

> airway disease and for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.
>
> 46. On October 1, 2022, the manufacturing of branded ProAir® HFA (albuterol sulfate) Inhalation Aerosol was discontinued. Teva USA currently distributes an authorized generic of ProAir® HFA (albuterol sulfate) Inhalation Aerosol under NDA No. 021457 in the United States.

Teva has thus premised this case on the factual allegation that the subject of NDA No. 021457 was the product, "ProAir® HFA (albuterol sulfate) Inhalation Aerosol." It is undisputed that no claim in any of the Inhaler Patents discloses albuterol sulfate.

The First Circuit construed the phrase, a patent which "claims the drug for which the applicant submitted the application," as used in § 355, in Cesar Castillo, Inc. v. Sanofi-Aventis U.S., LLC (In re Lantus Direct Purchaser Antitrust Litig.), 950 F.3d 1, 3 (1st Cir. 2020). Teva objects that, despite Lantus being a 2020 case, Congress has since changed the language of § 355 with the passage of the Orange Book Transparency Act ("OBTA"). Indeed, the OTBA did make changes to the language of § 355, but the key phrase, "claims the drug for which the applicant submitted the application," has not changed. At the time the First Circuit decided Lantus, the listing provision in § 355 required that the NDA applicant list a patent which "claims the drug for which the applicant submitted the application," and the current Listing Statute contains the same requirement today. Congress may have amended parts of the Listing Statute, but the OTBA did not change this particular requirement for listing a patent in the Orange Book: a listed patent must still claim the drug for which the applicant submitted the application.

In Lantus, Sanofi a filed a supplemental NDA "to sell insulin glargine in a disposable injector pen device called the Lantus SoloSTAR." Lantus, 950 F.3d at 5. The patent at issue, the '864 patent, was directed to drive mechanisms used in drug delivery devices. Id. In short,

the First Circuit found that the '864 patent did not claim the drug for which the applicant submitted the application. Id. at 8. Moreover, the First Circuit rejected the idea that § 355 authorizes the listing of "patents that claim only components of a proposed drug." Id. at 9. The Court concluded:

> More importantly, even assuming that the drive mechanism claimed by the '864 patent is itself a drug, we still find Sanofi falling short of its goal because the drive mechanism is not the "drug for which [Sanofi] submitted" the NDA. 21 U.S.C. § 355(b)(1). For that reason alone the patent for the drive mechanism does not qualify for listing in the Orange Book as claiming the Lantus SoloSTAR.
> . . .
> The statute and regulations clearly require that only patents that claim the drug for which the NDA is submitted should be listed in the Orange Book. The '864 patent, which neither claims nor even mentions insulin glargine or the Lantus SoloSTAR, does not fit the bill.

Id. at 9-10.

The facts of Lantus are parallel to those of the instant case. The Inhaler Patents are directed to components of a metered inhaler device, but do not claim or even mention albuterol sulfate or the ProAir® HFA. The applicant filed an NDA for an albuterol sulfate HFA Inhalation Aerosol. The statutory requirement that each patent "claim[] the drug for which the applicant submitted the application" is not met.

The FTC points out that the Second Circuit followed the relevant reasoning of Lantus in United Food & Commer. Workers Local 1776 v. Takeda Pharm. Co., 11 F.4th 118, 134 (2d Cir. 2021). United is a meaty opinion and much could be said about it, but two points are most relevant: 1) the Second Circuit decided United after passage of the OBTA and agreed with the pre-OBTA Lantus decision about the interpretation of "claims the drug for which the applicant submitted the application" in the Listing Statute; and 2) "claims" in the Listing Statute has the meaning established in patent law: "patent claims 'are the numbered paragraphs which

particularly point out and distinctly claim the subject matter which the applicant regards as his invention" (United, 11 F.4th at 132 (quoting Corning Glass Works v. Sumitomo Elec. U.S.A., Inc., 868 F.2d 1251, 1258 (Fed. Cir. 1989)). Applying the Second Circuit's analysis to the instant case, because the Inhaler Patents plainly do not regard an "albuterol sulfate HFA Inhalation Aerosol" as that which was invented, they do not claim the drug for which the applicant submitted the NDA application.

Teva offers two strategies that attempt to expand the scope of the key phrase in § 355, "claims the drug." First, Teva proffers a confusing set of arguments about the meaning of the word, "claims." Teva begins with the uncontroversial proposition that the word "claims" in the Listing Statute "should be given its meaning under patent law." (Pls.' MJP Opp. Br. at 13.) Somehow, Teva ends up at the position that "a patent 'claims' a product if the patent would be infringed by the product." (Id. at 15.) In support, Teva relies on the Second Circuit's decision in United Food. (Id.) The problem for Teva is that, as just stated, the Second Circuit in United Food based its entire analysis on this fundamental principle: "patent claims 'are the numbered paragraphs which particularly point out and distinctly claim the subject matter which the applicant regards as his invention." (United, 11 F.4th at 132 (quoting Corning Glass Works v. Sumitomo Elec. U.S.A., Inc., 868 F.2d 1251, 1258 (Fed. Cir. 1989)). Thus, a patent claims *only* that subject matter that it has particularly pointed out as the invention, and no more. This is inconsistent with Teva's contention that a patent claims all products that are infringing. Furthermore, the Second Circuit carefully explained the difference between the meaning of "claims" in patent law and "infringement." Id. at 134. In short, Teva has failed to persuade that, applying the common meaning of "claims" in patent law, any claim in any of the Inhaler

Patents particularly identifies the subject of the NDA application, an albuterol sulfate HFA Inhalation Aerosol, as the invention.

Second, Teva points to the broad statutory definition of "drug." The Court agrees with Teva that the statute, 21 U.S.C. § 321(g)(1), expressly gives the term, "drug," a broad scope, and specifically includes "articles intended for use as a component of any article" intended for use for the treatment of disease. Given the broad statutory definition of "drug," the Inhaler Patents do claim articles intended for use as a component of the ProAir® HFA (albuterol sulfate) Inhalation Aerosol, and it is undisputed that the albuterol sulfate HFA Inhalation Aerosol is intended for the treatment of disease. The problem for Teva is that this determination does not suffice to establish that the Inhaler Patents "claim[] the drug for which the applicant submitted the application," as required by the Listing Statute. Teva's arguments overlook the statutory phrase which modifies "drug:" "for which the applicant submitted the application." The drug for which the applicant submitted the application is "albuterol sulfate HFA Inhalation Aerosol." The Inhaler Patents do not contain any claims which claim "albuterol sulfate HFA Inhalation Aerosol." In short, the fact that the statutory definition of "drug" expressly includes devices for treating disease, and their components, does not nullify the restrictive action of the modifying phrase, "for which the applicant submitted the application." Teva tries hard to get around the effect of this modifying phrase, but fails to do so.

Lastly, as already noted, Teva maintains that the Inhaler Patents have been listed as "drug product" patents, within the meaning of § 355. The relevant Regulation defines "drug product" as follows: "Drug product is a finished dosage form, e.g., tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other

ingredients." 21 C.F.R. § 314.3(b). As the FTC observes, the Regulations also state: "For patents that claim a drug product, the applicant must submit information only on those patents that claim the drug product, as is defined in § 314.3, *that is described in the pending or approved NDA*." 21 C.F.R. § 314.53(b)(1)(italics added). The Inhaler Patents do not claim the "finished dosage form" that is the subject of NDA No. 021457.

Furthermore, the FTC cites a response to public comments made by the FDA during the 2003 rulemaking process for the Regulation, 21 C.F.R. § 314.53:

> (Comment 3) Most comments agreed that patents claiming packaging should not be submitted for listing. However, some comments stated that patents claiming devices or containers that are "integral" to the drug product or require prior FDA approval should be submitted and listed. These comments distinguished between packaging and devices such as metered dose inhalers and transdermal patches, which are drug delivery systems used and approved in combination with a drug.
>
> (Response) We agree that patents claiming a package or container must not be submitted. Such packaging and containers are distinct from the drug product and thus fall outside of the requirements for patent submission. However, we have clarified the rule to ensure that if the patent claims the drug product as defined in § 314.3, the patent must be submitted for listing.
>
> Section 314.3 defines a "drug product" as "* * * a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients." The appendix in the Orange Book lists current dosage forms for approved drug products. The list includes metered aerosols, capsules, metered sprays, gels, and pre-filled drug delivery systems. *The key factor is whether the patent being submitted claims the finished dosage form of the approved drug product.* Patents must not be submitted for bottles or containers and other packaging, as these are not "dosage forms."

68 Fed. Reg. 36676, 36680 (italics added). The Inhaler Patents do not claim the finished dosage form of the approved drug product.

The Court concludes that the Inhaler Patents do not meet a key requirement of the Listing Statute: they do not claim "the drug for which the applicant submitted the application," NDA No.

021457, ProAir® HFA (albuterol sulfate) Inhalation Aerosol. Nor do the Inhaler Patents claim the "finished dosage form" that is the subject of that NDA application. Because the Inhaler Patents fail to meet these requirements, that have been improperly listed in the Orange Book.

As to Counterclaim Counts 1-5, Teva's motion to dismiss will be denied. Amneal has demonstrated that, on the basis of the pleadings, it is entitled to judgment as a matter of law on Counterclaim Counts 1-5. Amneal's motion for judgment on the pleadings will be granted.

For these reasons,

IT IS on this 10th day of June, 2024

ORDERED that Plaintiff's motion to dismiss Counterclaim Counts 1-10 (Docket Entry No. 26) is **DENIED**; and it is further

ORDERED that Defendant's motion for partial judgment on the pleadings (Docket Entry No. 41) is **GRANTED**; and it is further

ORDERED that Judgment is entered in Defendants' favor as to Counts 1-5 of Defendants' Counterclaims; and it is further

ORDERED that it is the Judgment of this Court that U.S. Patent Nos. 8,132,712, 9,463,289, 9,808,587, 10,561,808, and 11,395,889 have been improperly listed in the Orange Book in regard to the drug product that is the subject of NDA No. 021457; and it is further

ORDERED that, pursuant to 21 U.S.C. § 355(j)(5)(c)(ii)(I), Teva must correct or delete the relevant Orange Book patent information listings to reflect the Judgment of this Court.

/s Stanley R. Chesler
STANLEY R. CHESLER. U.S.D.J.

ANDA,APPEAL,SCHEDO

U.S. District Court
District of New Jersey [LIVE] (Newark)
CIVIL DOCKET FOR CASE #: 2:23-cv-20964-SRC-MAH

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC. et al v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC et al
Assigned to: Judge Stanley R. Chesler
Referred to: Magistrate Judge Michael A. Hammer
Related Cases: 2:24-cv-00909-SRC-MAH
2:24-cv-04404-SRC-MAH
Case in other court: Federal Circuit, 24-01936
Cause: 35:271 Patent Infringement

Date Filed: 10/06/2023
Jury Demand: Defendant
Nature of Suit: 835 Patent - Abbreviated New Drug Application(ANDA)
Jurisdiction: Federal Question

Plaintiff

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC.

represented by

CHRISTINE CLARK
WALSH PIZZI O'REILLY FALANGA LLP
THREE GATEWAY CENTER
100 MULBERRY STREET, 15TH FLOOR
NEWARK, NJ 07012
973-757-1100
Email: cclark@walsh.law
ATTORNEY TO BE NOTICED

HECTOR DANIEL RUIZ
WALSH PIZZI O'REILLY FALANGA LLP
THREE GATEWAY CENTER
100 MULBERRY STREET
15TH FLOOR
NEWARK, NJ 07102
973.757.1100
Email: hruiz@walsh.law
ATTORNEY TO BE NOTICED

SELINA MIRIAM ELLIS
WALSH PIZZI O'REILLY FALANGA LLP
THREE GATEWAY CENTER
100 MULBERRY STREET
15TH FLOOR
NEWARK, NJ 07102
973-757-1100
Email: sellis@walsh.law
ATTORNEY TO BE NOTICED

LIZA M. WALSH
WALSH PIZZI O'REILLY FALANGA LLP
THREE GATEWAY CENTER
100 MULBERRY STREET
15TH FLOOR
NEWARK, NJ 07102
973.757.1100
Email: lwalsh@walsh.law
ATTORNEY TO BE NOTICED

Plaintiff

NORTON (WATERFORD) LTD. represented by **CHRISTINE CLARK**
(See above for address)
ATTORNEY TO BE NOTICED

HECTOR DANIEL RUIZ
(See above for address)
ATTORNEY TO BE NOTICED

SELINA MIRIAM ELLIS
(See above for address)
ATTORNEY TO BE NOTICED

LIZA M. WALSH
(See above for address)
ATTORNEY TO BE NOTICED

Plaintiff

TEVA PHARMACEUTICALS USA, INC. represented by **CHRISTINE CLARK**
(See above for address)
ATTORNEY TO BE NOTICED

HECTOR DANIEL RUIZ
(See above for address)
ATTORNEY TO BE NOTICED

SELINA MIRIAM ELLIS
(See above for address)
ATTORNEY TO BE NOTICED

LIZA M. WALSH
(See above for address)
ATTORNEY TO BE NOTICED

V.

Defendant

AMNEAL PHARMACEUTICALS OF NEW YORK, LLC represented by **SHALOM D STONE**
STONE CONROY LLC
25A HANOVER ROAD
SUITE 301
FLORHAM PARK, NJ 07932
(973) 400-4181
Fax: (973) 498-0070
Email: sstone@stoneconroy.com
ATTORNEY TO BE NOTICED

REBEKAH R. CONROY
STONE CONROY LLC
25A HANOVER ROAD
SUITE 301
FLORHAM PARK, NJ 07932
(973) 400-4181
Fax: (973) 498-0070
Email: rconroy@stoneconroy.com
ATTORNEY TO BE NOTICED

Defendant

AMNEAL IRELAND LIMITED represented by **SHALOM D STONE**
(See above for address)
ATTORNEY TO BE NOTICED

REBEKAH R. CONROY
(See above for address)
ATTORNEY TO BE NOTICED

Defendant

AMNEAL PHARMACEUTICALS LLC represented by **SHALOM D STONE**
(See above for address)
ATTORNEY TO BE NOTICED

REBEKAH R. CONROY
(See above for address)
ATTORNEY TO BE NOTICED

Defendant

AMNEAL PHARMACEUTICALS INC. represented by **SHALOM D STONE**
(See above for address)
LEAD ATTORNEY
ATTORNEY TO BE NOTICED

REBEKAH R. CONROY
(See above for address)
ATTORNEY TO BE NOTICED

Defendant

PHV ROBIN P. SUMNER represented by **ROBIN P. SUMNER**
Email: robin.sumner@troutman.com
PRO SE

Amicus

FEDERAL TRADE COMMISSION
U.S. Federal Trade Commission
600 Pennsylvania Ave., N.W.
Washington, DC 20580
2023862652
represented by **BRADLEY VETTRAINO**
FEDERAL TRADE COMMISSION
600 PENNSYLVANIA AVE., N.W.
WASHINGTON, DC 20580
202-386-2652
Email: bvettraino@ftc.gov
LEAD ATTORNEY
ATTORNEY TO BE NOTICED

Counter Claimant

AMNEAL PHARMACEUTICALS LLC represented by **REBEKAH R. CONROY**
(See above for address)
ATTORNEY TO BE NOTICED

Counter Claimant

AMNEAL PHARMACEUTICALS OF NEW YORK, LLC represented by **REBEKAH R. CONROY**
(See above for address)
ATTORNEY TO BE NOTICED

Counter Claimant

AMNEAL PHARMACEUTICALS INC. represented by **REBEKAH R. CONROY**
(See above for address)
ATTORNEY TO BE NOTICED

Counter Claimant

AMNEAL IRELAND LIMITED represented by **REBEKAH R. CONROY**
(See above for address)
ATTORNEY TO BE NOTICED

V.

Counter Defendant

NORTON (WATERFORD) LTD. represented by **SELINA MIRIAM ELLIS**
(See above for address)
ATTORNEY TO BE NOTICED

LIZA M. WALSH
(See above for address)
ATTORNEY TO BE NOTICED

Counter Defendant

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC. represented by **SELINA MIRIAM ELLIS**
(See above for address)
ATTORNEY TO BE NOTICED

LIZA M. WALSH
(See above for address)
ATTORNEY TO BE NOTICED

Counter Defendant

TEVA PHARMACEUTICALS USA, INC. represented by **SELINA MIRIAM ELLIS**
(See above for address)
ATTORNEY TO BE NOTICED

LIZA M. WALSH
(See above for address)
ATTORNEY TO BE NOTICED

Date Filed	#	Docket Text
10/06/2023	1	COMPLAINT against AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC (Filing and Admin fee $ 402 receipt number ANJDC-14771159) , *Related Case Selected*, filed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC., NORTON (WATERFORD) LTD.. (Attachments: # 1 Exhibit A-C, # 2 Exhibit D-F, # 3 Civil Cover Sheet, # 4 AO120 Form I, # 5 Ao 120 Form II)(WALSH, LIZA) (Entered: 10/06/2023)
10/06/2023	2	Corporate Disclosure Statement by NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC.. (WALSH, LIZA) (Entered: 10/06/2023)
10/10/2023		Case assigned to Judge Claire C. Cecchi and Magistrate Judge James B. Clark. (jr) (Entered: 10/10/2023)
10/11/2023	3	AO120 Patent/Trademark Form filed. (Attachments: # 1 Complaint and Exhibits) (jd,) (Entered: 10/11/2023)
10/11/2023	4	SUMMONS ISSUED as to AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. Attached is the official court Summons, please fill out Defendant and Plaintiffs attorney information and serve. (jd,) (Entered: 10/11/2023)
10/13/2023	5	TEXT ORDER REASSIGNING CASE. Case reassigned to Judge Julien Xavier Neals and Magistrate Judge Michael A. Hammer for all further proceedings. Judge Claire C. Cecchi, Magistrate Judge James B. Clark no longer assigned to case. So Ordered by Chief Judge Renee Marie Bumb on 10/13/23. (ak,) (Entered: 10/13/2023)
10/16/2023	6	NOTICE of Appearance by SELINA MIRIAM ELLIS on behalf of NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC. (ELLIS, SELINA) (Entered: 10/16/2023)

10/16/2023		Notice of Judicial Preferences. Click here for the Judge's Individual Procedure Requirements. (kd) (Entered: 10/16/2023)
10/27/2023	7	AMENDED COMPLAINT against AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, filed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC., NORTON (WATERFORD) LTD.. (Attachments: # 1 Exhibit A-E)(WALSH, LIZA) (Entered: 10/27/2023)
10/30/2023	8	TEXT ORDER: Plaintiff shall mail a tabbed courtesy copy of the Amended Complaint 7 to Chambers by 11/6/2023. So Ordered by Magistrate Judge Michael A. Hammer on 10/30/2023. (jqb,) (Entered: 10/30/2023)
11/09/2023	9	ACKNOWLEDGMENT OF SERVICE Executed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC., NORTON (WATERFORD) LTD.. (WALSH, LIZA) (Entered: 11/09/2023)
11/09/2023	10	STIPULATION *AND [PROPOSED] ORDER FOR EXTENSION OF TIME* by NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC.. (WALSH, LIZA) (Entered: 11/09/2023)
11/13/2023	11	STIPULATION AND ORDER granting Defendants AMNEAL request for an extension of time to answer, move, or otherwise respond to Plaintiff's First Amended Complaint in this action, until 12/1/2023. Signed by Magistrate Judge Michael A. Hammer on 11/13/2023. (jd,) (Entered: 11/13/2023)
12/01/2023	12	*DEFENDANTS'* ANSWER to Amended Complaint , *Affirmative Defenses and*, COUNTERCLAIM against NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC. by AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL PHARMACEUTICALS INC., AMNEAL IRELAND LIMITED. (Attachments: # 1 Exhibit Exh. A, # 2 Exhibit Exh. B, # 3 Exhibit Exh. C, # 4 Exhibit Exh. D, # 5 Exhibit Exh. E, # 6 Exhibit Exh. F, # 7 Exhibit Exh. G, # 8 Exhibit Exh. H, # 9 Exhibit Exh. I, # 10 Exhibit Exh. J, # 11 Exhibit Exh. K, # 12 Exhibit Exh. L, # 13 Exhibit Exh. M, # 14 Exhibit Exh. N, # 15 Exhibit Exh. O, # 16 Exhibit Exh. P, # 17 Exhibit Exh. Q, # 18 Exhibit Exh. R, # 19 Exhibit Exh. S, # 20 Exhibit Exh. T, # 21 Exhibit Exh. U, # 22 Exhibit Exh. V, # 23 Exhibit Exh. W, # 24 Exhibit Exh. X)(CONROY, REBEKAH) (Entered: 12/01/2023)
12/01/2023	13	Corporate Disclosure Statement by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (CONROY, REBEKAH) (Entered: 12/01/2023)
12/19/2023	14	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. re 12 Answer to Amended Complaint,,,, Counterclaim,,,. (WALSH, LIZA) (Entered: 12/19/2023)
12/20/2023	15	LETTER ORDER granting 14 Plaintiffs' Request for an extension from 12/22/2023 until 1/26/2024 to answer or otherwise respond to Defendants' Counterclaims (D.E. 12). Signed by Magistrate Judge Michael A. Hammer on 12/20/2023. (dam) (Main Document 15 replaced on 12/20/2023) (dam,). (Entered: 12/20/2023)
12/20/2023		CLERK'S QUALITY CONTROL MESSAGE - Please be advised that the document attached to 15 Letter Order filed by the Clerk's Office on 12/20/2023 was attached in error. The Clerk's Office has replaced the document with the correct version. This message is for informational purposes. This submission will remain on the docket unless otherwise ordered by the court. (dam) (Entered: 12/20/2023)
12/28/2023	16	TEXT ORDER REASSIGNING CASE. Case reassigned to Judge Jamel K. Semper for all further proceedings. Judge Julien Xavier Neals no longer assigned to case. So Ordered by Chief Judge Renee Marie Bumb on 12/28/2023. (adc,) (Entered: 12/28/2023)
01/07/2024	17	TEXT ORDER: Telephone Scheduling Conference set for 2/7/2024 at 4:30 p.m. The parties will dial 1-888-684-8852 and access code 1456817# to join the conference. The parties file a joint discovery plan by 2/5/2024. So Ordered by Magistrate Judge Michael A. Hammer on 1/7/2024. (jqb,) (Entered: 01/07/2024)
01/12/2024	18	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. encl. Pro Hac Vice Application on Consent. (Attachments: # 1 Certification of Liza M. Walsh, # 2 Certification of Christopher T.

		Holding, # 3 Certification of Daryl L. Wiesen, # 4 Certification of Natasha E. Daughtrey, # 5 Certification of Louis L. Lobel, # 6 Certification of Thomas V. McTigue IV, # 7 Text of Proposed Order)(WALSH, LIZA) (Entered: 01/12/2024)
01/12/2024	19	TEXT ORDER REASSIGNING CASE. Case reassigned to Judge Stanley R. Chesler for all further proceedings. Judge Jamel K. Semper no longer assigned to case. So Ordered by Chief Judge Renee Marie Bumb on 1/12/2024. (smf) (Entered: 01/12/2024)
01/12/2024		Set/Reset Hearings: Status Conference set for 1/17/2024 at 01:00 PM before Judge Stanley R. Chesler. ORDERED TRIAL COUNSEL WITH FULL SETTLEMENT AUTHORITY ALONG WITH LOCAL COUNSEL MUST APPEAR IN PERSON. (tt,) (Entered: 01/12/2024)
01/16/2024	20	CONSENT ORDER granting 18 the application for the pro hac vice admission of attorneys CHRISTOPHER T. HOLDING, DARYL L. WIESEN, NATASHA E. DAUGHTREY, LOUIS L. LOBEL, and THOMAS V. MCTIGUE IV. Signed by Magistrate Judge Michael A. Hammer on 1/16/2024. (jd,) (Entered: 01/16/2024)
01/16/2024		Set/Reset Hearings: Status Conference set for 3/5/2024 at 10:00 AM before Judge Stanley R. Chesler. ORDERED TRIAL COUNSEL WITH FULL SETTLEMENT AUTHORITY ALONG WITH LOCAL COUNSEL MUST APPEAR IN PERSON. (tt,) (Entered: 01/16/2024)
01/17/2024	21	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. re 17 Order,, Set/Clear Flags,. (WALSH, LIZA) (Entered: 01/17/2024)
01/18/2024	22	TEXT ORDER: At the request of Plaintiffs' Counsel, the Rule 16 scheduling conference is adjourned to February 21, 2024 at 3:30 p.m. The conference will be held in person in Courtroom 2C in the Martin Luther King Building and U.S. Courthouse. The parties shall file their joint discovery plan not later than February 16, 2024. So Ordered by Magistrate Judge Michael A. Hammer on 1/18/24. (tad) (Entered: 01/18/2024)
01/24/2024	23	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J.. (WALSH, LIZA) (Entered: 01/24/2024)
01/25/2024	24	Letter from Defendant Amneal Pharmaceuticals LLC to the Hon. Michael A. Hammer, U.S.M.J. re 23 Letter. (Attachments: # 1 Exhibit Exhibit 1, # 2 Exhibit Exhibit 2, # 3 Exhibit Exhibit 3, # 4 Exhibit Exhibit 4, # 5 Exhibit Exhibit 5)(CONROY, REBEKAH) (Entered: 01/25/2024)
01/26/2024	25	TEXT ORDER: The Court has considered Teva's January 24, 2024 letter request to file its answer to the counterclaims until after the District Court rules on Teva's motion to dismiss certain of those counterclaims, pursuant to Local Civil Rule 12.2. The Court also has considered Amneal's January 25, 2024 letter setting forth its objections to Teva's proposal, and requesting that Amneal be permitted to proceed now on its anticipated Rule 12(c) motion. In the interest of judicial efficiency, and it appearing that the subject matter of Teva's Rule 12(b)(6) motion and the subject matter of Amneal's anticipated Rule 12(c) motion will likely overlap, and that both Teva's Rule 12(b)(6) motion and Amneal's Rule 12(c) motion will apply the same legal standard: (1) Teva's request is granted. Teva shall file the answer to all remaining counterclaims upon resolution of the Rule 12(b)(6) motion; and (2) Amneal may proceed at this time with its Rule 12(c) motion. To the extent Teva posits that Amneal's Rule 12(c) motion must await closure of the operative pleadings, that assertion is not well taken. It is well settled that the Court has the discretion to structure Rule 12 motion practice so as to promote timely and efficient resolution of the pleadings, and secure the just and speedy resolution of litigation particularly where, as here, there is likely significant overlap in the subject matter of the anticipated motions and the legal standard is virtually identical. See Fed. R. Civ. P. 1, 16 The Court also is not persuaded that Amneal's Rule 12(c) motion necessarily requires an answer to the de-listing counterclaims. Finally, the February 21, 2024 in-person Rule 16 conference shall proceed as scheduled. So Ordered by Magistrate Judge Michael A. Hammer on 1/26/2024. (Hammer, Michael) (Entered: 01/26/2024)
01/26/2024		Pro Hac Vice fee received for Christopher T. Holding, Daryl L. Wiesen, Natasha E. Daughtrey, Louis L. Lobel and Thomas V. McTigue IV: $ 750, receipt number 136721 (jjc,) (Entered: 01/26/2024)
01/26/2024	26	MOTION to Dismiss *DEFENDANTS' COUNTERCLAIM COUNTS 1-10* by NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC.. (Attachments: # 1 Declaration of Liza M. Walsh, # 2 Exhibit 2, # 3 Exhibit 3, # 4 Text of Proposed Order)(WALSH, LIZA) (Entered: 01/26/2024)

01/26/2024	27	BRIEF in Support filed by NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC. re 26 MOTION to Dismiss *DEFENDANTS' COUNTERCLAIM COUNTS 1-10 (Under Seal)* (Attachments: # 1 Exhibit 1 (Under Seal))(WALSH, LIZA) NOTICE TO COUNSEL: Counsel is advised that pursuant to Local Civil Rule 5.3(c)(2), a single, consolidated motion to seal shall be filed within 14 days following the completed briefing of the materials sought to be sealed, or within 14 days following the date on which the last of such materials was filed under temporary seal if the motion is resolved, unless otherwise directed by the Court. (Entered: 01/26/2024)
01/29/2024	28	REDACTION to 27 Brief in Support of Motion,, by NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC.. (WALSH, LIZA) (Entered: 01/29/2024)
01/29/2024	29	Notice of Request by Pro Hac Vice Christopher T. Holding to receive Notices of Electronic Filings. (WALSH, LIZA) (Entered: 01/29/2024)
01/29/2024	30	Notice of Request by Pro Hac Vice Daryl L. Wiesen to receive Notices of Electronic Filings. (WALSH, LIZA) (Entered: 01/29/2024)
01/29/2024	31	Notice of Request by Pro Hac Vice Natasha E. Daughtrey to receive Notices of Electronic Filings. (WALSH, LIZA) (Entered: 01/29/2024)
01/29/2024	32	Notice of Request by Pro Hac Vice Louis L. Lobel to receive Notices of Electronic Filings. (WALSH, LIZA) (Entered: 01/29/2024)
01/29/2024	33	Notice of Request by Pro Hac Vice Thomas V. McTigue IV to receive Notices of Electronic Filings. (WALSH, LIZA) (Entered: 01/29/2024)
01/29/2024		Set Deadlines as to 26 MOTION to Dismiss DEFENDANTS' COUNTERCLAIM COUNTS 1-10. Motion set for 2/20/2024 before Judge Stanley R. Chesler. Unless otherwise directed by the Court, this motion will be decided on the papers and no appearances are required. Note that this is an automatically generated message from the Clerk`s Office and does not supersede any previous or subsequent orders from the Court. (jd,) (Entered: 01/29/2024)
01/31/2024		Pro Hac Vice counsel, CHRISTOPHER T. HOLDING, DARYL L. WIESEN, NATASHA E. DAUGHTREY, LOUIS L. LOBEL and THOMAS MCTIGUE, has been added to receive Notices of Electronic Filing. Pursuant to L.Civ.R. 101.1, only local counsel are entitled to sign and file papers, enter appearances and receive payments on judgments, decrees or orders. (jd,) (Entered: 01/31/2024)
02/06/2024	34	Letter from Defendants on Behalf of All Parties to the Hon. Michael A. Hammer, U.S.M.J.. (CONROY, REBEKAH) (Entered: 02/06/2024)
02/07/2024	35	LETTER ORDER granting 34 Joint consolidated briefing schedule and page limits for Plaintiffs'. Signed by Magistrate Judge Michael A. Hammer on 2/7/2024. (jd,) (Entered: 02/08/2024)
02/09/2024	36	NOTICE of Appearance by HECTOR DANIEL RUIZ on behalf of NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC. (RUIZ, HECTOR) (Entered: 02/09/2024)
02/09/2024	37	NOTICE of Appearance by CHRISTINE CLARK on behalf of NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC. (CLARK, CHRISTINE) (Entered: 02/09/2024)
02/14/2024	38	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. encl. Joint Discovery Plan. (Attachments: # 1 Joint Discovery Plan)(WALSH, LIZA) (Entered: 02/14/2024)
02/16/2024	39	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J.. (CLARK, CHRISTINE) (Entered: 02/16/2024)
02/20/2024	40	TEXT ORDER: The Court has reviewed the parties' February 16, 2024 letter [D.E. 39], which requests that the February 21st Rule 16 conference proceed via telephonically. In an effort to accommodate counsel, and in view of there being no disputes at this time, the conference shall proceed via Microsoft Teams at the same time. The Court will provide the Teams link to counsel. So Ordered by Magistrate Judge Michael A. Hammer on 2/20/2024. (Hammer, Michael) (Entered: 02/20/2024)

02/20/2024	41	MOTION for Judgment on the Pleadings *as to Counterclaims 1-5* by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (Attachments: # 1 Declaration of Rebekah Conroy, # 2 Exhibit 1 to Conroy Decl., # 3 Exhibit 2 to Conroy Decl., # 4 Exhibit 3 to Conroy Decl., # 5 Exhibit 4 to Conroy Decl., # 6 Exhibit 5 to Conroy Decl., # 7 Exhibit 6 to Conroy Decl., # 8 Exhibit 7 to Conroy Decl., # 9 Exhibit 8 to Conroy Decl., # 10 Exhibit 9 to Conroy Decl., # 11 Exhibit 10 to Conroy Decl., # 12 Exhibit 11 to Conroy Decl., # 13 Exhibit 12 to Conroy Decl., # 14 Text of Proposed Order Granting Motion for Judgment on the Pleadings as to Counterclaims 1-5)(CONROY, REBEKAH) (Entered: 02/20/2024)
02/20/2024	42	BRIEF in Support filed by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC re 26 MOTION to Dismiss *DEFENDANTS' COUNTERCLAIM COUNTS 1-10*, 41 MOTION for Judgment on the Pleadings *as to Counterclaims 1-5 and in Opposition to Plaintiffs' Motion to Dismiss* (CONROY, REBEKAH) NOTICE TO COUNSEL: Counsel is advised that pursuant to Local Civil Rule 5.3(c)(2), a single, consolidated motion to seal shall be filed within 14 days following the completed briefing of the materials sought to be sealed, or within 14 days following the date on which the last of such materials was filed under temporary seal if the motion is resolved, unless otherwise directed by the Court. (Entered: 02/20/2024)
02/21/2024		Set Deadlines as to 41 MOTION for Judgment on the Pleadings as to Counterclaims 1-5. Motion set for 3/18/2024 before Judge Stanley R. Chesler. Unless otherwise directed by the Court, this motion will be decided on the papers and no appearances are required. Note that this is an automatically generated message from the Clerk`s Office and does not supersede any previous or subsequent orders from the Court. (jd,) (Entered: 02/21/2024)
02/21/2024	43	PRETRIAL SCHEDULING ORDER. Signed by Magistrate Judge Michael A. Hammer on 2/21/2024. (jd,) (Entered: 02/22/2024)
02/21/2024		Minute Entry for proceedings held before Magistrate Judge Michael A. Hammer: Scheduling Conference held on 2/21/2024. (ECR) (jqb,) (Entered: 02/22/2024)
02/22/2024	44	Letter from Defendants with Consent of All Parties re 35 Order. (CONROY, REBEKAH) (Entered: 02/22/2024)
02/23/2024	45	LETTER ORDER granting 44 Defendant's request for a one-week extension to the briefing schedule for the pending motions. Signed by Magistrate Judge Michael A. Hammer on 2/22/2024. (jd,) Modified on 2/23/2024 (jd,). (Entered: 02/23/2024)
02/26/2024	46	Letter from Liza M. Walsh, Esq. to the Hon. Michael A. Hammer, U.S.M.J... (WALSH, LIZA) (Entered: 02/26/2024)
02/27/2024	47	TEXT ORDER: There will be a telephone conference today at 4:00 p.m. to discuss the parties' February 26, 2024 proposal to extend the deadline to serve written discovery until thirty days before the close of fact discovery. Counsel will dial 1-888-684-8852 and enter 1456817# to join the conference. So Ordered by Magistrate Judge Michael A. Hammer on 2/27/2024. (Hammer, Michael) (Entered: 02/27/2024)
02/27/2024	48	REDACTION to 42 Brief in Support of Motion,,, *Redacted Memorandum of Law* by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (CONROY, REBEKAH) (Entered: 02/27/2024)
02/27/2024	49	TEXT ORDER: As discussed during today's telephone conference, the parties shall meet and confer and file a proposed amended scheduling order not later than March 8, 2024. So Ordered by Magistrate Judge Michael A. Hammer on 2/27/24. (tad) (Entered: 02/27/2024)
02/27/2024		Minute Entry for proceedings held before Magistrate Judge Michael A. Hammer: Status Conference held on 2/27/2024. (ECR) (jqb,) (Entered: 02/27/2024)
03/05/2024	50	Minute Entry for proceedings held before Judge Stanley R. Chesler: Status Conference held on 3/5/2024. Local and Trial Counsel present. Pro hac vice for defendants shall be filed. (tt,) (Entered: 03/05/2024)

03/05/2024	51	MOTION for Leave to File *Motion for Leave to File as Amicus by March 22, 2024* by FEDERAL TRADE COMMISSION. (Attachments: # 1 Text of Proposed Order Proposed Order)(VETTRAINO, BRADLEY) (Entered: 03/05/2024)
03/06/2024	52	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. encl. Proposed Stipulated Discovery Confidentiality Order. (Attachments: # 1 Text of Proposed Order, # 2 Declaration of Liza M. Walsh, # 3 Declaration of Rebekah Conroy)(WALSH, LIZA) (Entered: 03/06/2024)
03/07/2024		Set Deadlines as to 51 MOTION for Leave to File Motion for Leave to File as Amicus by March 22, 2024. Motion set for 4/1/2024 before Magistrate Judge Michael A. Hammer. Unless otherwise directed by the Court, this motion will be decided on the papers and no appearances are required. Note that this is an automatically generated message from the Clerk`s Office and does not supersede any previous or subsequent orders from the Court. (jd,) (Entered: 03/07/2024)
03/07/2024	53	Discovery Confidentiality Order. Signed by Magistrate Judge Michael A. Hammer on 3/7/2024. (jd,) (Entered: 03/07/2024)
03/08/2024	54	ORDER granting the Federal Trade Commission's 51 Motion for Leave to File a Motion Seeking Leave to File an Amicus Brief. Signed by Judge Stanley R. Chesler on 3/8/2024. (mxw,) (Entered: 03/08/2024)
03/08/2024	55	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. re 49 Order. (Attachments: # 1 Text of Proposed Order)(WALSH, LIZA) (Entered: 03/08/2024)
03/11/2024	56	AMENDED PRETRIAL SCHEDULING ORDER. Signed by Magistrate Judge Michael A. Hammer on 3/11/2024. (jd,) (Entered: 03/11/2024)
03/11/2024	57	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. re briefing schedule. (CLARK, CHRISTINE) (Entered: 03/11/2024)
03/12/2024	58	LETTER ORDER granting 57 the parties request to modify the briefing schedule. TEVA's consolidated opposition papers to AMNEAL'S motion and reply brief due on 4/15/2024. Signed by Magistrate Judge Michael A. Hammer on 3/12/2024. (jd,) (Entered: 03/12/2024)
03/13/2024	59	Letter from Defendants Seeking Pro Hac Vice Admission of Counsel with Consent. (Attachments: # 1 Certification of Rebekah Conroy, # 2 Certification of Jeremy J. Edwards, # 3 Certification of Steven A. Maddox, # 4 Certification of Melissa Hatch O'Donnell, # 5 Certification of Robin P. Sumner, # 6 Certification of Andrew P. Zappia, # 7 Text of Proposed Order Admitting Counsel Pro Hac Vice by Consent)(CONROY, REBEKAH) (Entered: 03/13/2024)
03/13/2024	60	ORDER granting 59 Application for the admission of pro hac vice Attorneys JEREMY J. EDWARDS, STEVEN A. MADDOX, MELISSA HATCH O'DONNELL, ROBIN P. SUMNER, and ANDREW P. ZAPPIA. Signed by Magistrate Judge Michael A. Hammer on 3/13/2024.(jd,) Modified on 3/13/2024 (jd,). (Entered: 03/13/2024)
03/21/2024	62	Transcript of Hearing held on February 21, 2024, before Magistrate Judge Michael A. Hammer. Transcriber: King Transcription Services (973-237-6080). **NOTICE REGARDING (1) REDACTION OF PERSONAL IDENTIFIERS IN TRANSCRIPTS AND (2) MOTION TO REDACT AND SEAL:** The parties have seven (7) calendar days to file with the Court a Notice of Intent to Request Redaction of this Transcript to comply with Fed.R.Civ.P.5.2(a) (personal identifiers). Parties seeking to redact and seal this Transcript, or portions thereof, pursuant to L.Civ.R. 5.3(g) must e-file a Motion to Redact and Seal utilizing the event `Redact and Seal Transcript/Digital Recording`. Redaction Request to Transcription Agency due, but not filed, by 4/11/2024. Redacted Transcript Deadline set for 4/22/2024. Release of Transcript Restriction set for 6/20/2024. (jml) (Entered: 03/22/2024)
03/22/2024	61	Consent MOTION for Leave to File *Brief as Amicus Curiae* by FEDERAL TRADE COMMISSION. (Attachments: # 1 Proposed Amicus Brief, # 2 Text of Proposed Order)(VETTRAINO, BRADLEY) (Entered: 03/22/2024)
03/25/2024		Set Deadlines as to 61 Consent MOTION for Leave to File Brief as Amicus Curiae. Motion set for 4/15/2024 before Magistrate Judge Michael A. Hammer. Unless otherwise directed by the Court, this motion will be decided on the papers and no appearances are required. Note that this is an automatically generated message from the Clerk`s Office and does not supersede any previous or subsequent orders from the Court. (jd,) (Entered: 03/25/2024)

03/28/2024	63	ORDER granting 61 The Federal Trade Commission's Motion for Leave to File as Amicus Curiae. Signed by Magistrate Judge Michael A. Hammer on 3/28/2024. (jd,) (Entered: 03/28/2024)
04/15/2024	64	BRIEF in Opposition filed by All Plaintiffs re 41 MOTION for Judgment on the Pleadings *as to Counterclaims 1-5 AND REPLY IN SUPPORT OF PLAINTIFFS MOTION TO DISMISS* (Attachments: # 1 Declaration of Liza M. Walsh, # 2 Exhibit 11)(CLARK, CHRISTINE) NOTICE TO COUNSEL: Counsel is advised that pursuant to Local Civil Rule 5.3(c)(2), a single, consolidated motion to seal shall be filed within 14 days following the completed briefing of the materials sought to be sealed, or within 14 days following the date on which the last of such materials was filed under temporary seal if the motion is resolved, unless otherwise directed by the Court. (Entered: 04/15/2024)
04/15/2024	65	Exhibit to 64 Brief in Opposition to Motion,, *Exhibits 4, 5, 6, 7, 8, 9, and 10* by All Plaintiffs. (CLARK, CHRISTINE) (Entered: 04/15/2024)
04/15/2024	66	Certification of Service of Liza M. Walsh on behalf of All Plaintiffs Re 64 Brief in Opposition to Motion,, 65 Exhibit (to Document). (CLARK, CHRISTINE) (Entered: 04/15/2024)
04/26/2024	67	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J.. (WALSH, LIZA) (Entered: 04/26/2024)
04/29/2024	68	LETTER ORDER granting 67 Plaintiff's request to modify the Amended Pretrial Scheduling Order. Signed by Magistrate Judge Michael A. Hammer on 4/29/2024. (jd,) (Entered: 04/29/2024)
05/02/2024	69	REDACTION to 64 Brief in Opposition to Motion,, by All Plaintiffs. (Attachments: # 1 (Redacted) Declaration of L. Walsh)(WALSH, LIZA) (Entered: 05/02/2024)
05/07/2024	70	REPLY BRIEF to Opposition to Motion filed by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC re 41 MOTION for Judgment on the Pleadings *as to Counterclaims 1-5* (CONROY, REBEKAH) (Entered: 05/07/2024)
05/07/2024		Set/Reset Deadlines as to 26 MOTION to Dismiss *DEFENDANTS' COUNTERCLAIM COUNTS 1-10*, 41 MOTION for Judgment on the Pleadings *as to Counterclaims 1-5*. Motion set for 5/14/2024 at 10:00 AM in Newark - Courtroom 2 before Judge Stanley R. Chesler. ORDERED ALL PARTIES TO APPEAR IN PERSON READY TO PROCEED (tt,) (Entered: 05/07/2024)
05/09/2024		Set/Reset Deadlines as to 26 MOTION to Dismiss *DEFENDANTS' COUNTERCLAIM COUNTS 1-10*, 41 MOTION for Judgment on the Pleadings *as to Counterclaims 1-5*. Motion set for 5/22/2024 at 10:00 AM in Newark - Courtroom 2 before Judge Stanley R. Chesler. ORDERED ALL PARTIES TO APPEAR READY TO PROCEED (tt,) (Entered: 05/09/2024)
05/13/2024	71	MOTION for Leave to Appear Pro Hac Vice *Kathryn S. Kayali* by All Plaintiffs. (Attachments: # 1 Certification of Kathryn S. Kayali, # 2 Certification of Liza M. Walsh, # 3 Text of Proposed Order) (WALSH, LIZA) (Entered: 05/13/2024)
05/14/2024	72	TEXT ORDER: In light of the recent amendments to the Amended Pretrial Scheduling Order, D.E. 68, the telephone conference set for May 20, 2024 is adjourned to August 15, 2024 at 3:00 p.m. Counsel shall dial 1-888-684-8852 and enter access code 1456817# to join the call. So Ordered by Magistrate Judge Michael A. Hammer on 5/14/24. (tad) (Entered: 05/14/2024)
05/14/2024	73	CONSENT ORDER granting 71 Motion for Leave to Appear Pro Hac Vice as to KATHRYN S. KAYALI. Signed by Magistrate Judge Michael A. Hammer on 5/14/2024. (jd,) (Entered: 05/14/2024)
05/14/2024	74	Notice of Request by Pro Hac Vice Andrew P. Zappia, Esq. to receive Notices of Electronic Filings. (Pro Hac Vice fee $ 250 receipt number ANJDC-15366306.) (CONROY, REBEKAH) (Entered: 05/14/2024)
05/14/2024	75	Notice of Request by Pro Hac Vice Brett Garrrison to receive Notices of Electronic Filings. (Pro Hac Vice fee $ 250 receipt number ANJDC-15366333.) (CONROY, REBEKAH) (Entered: 05/14/2024)
05/14/2024	76	Notice of Request by Pro Hac Vice Jeremy Edwards, Esq. to receive Notices of Electronic Filings. (Pro Hac Vice fee $ 250 receipt number ANJDC-15366343.) (CONROY, REBEKAH) (Entered: 05/14/2024)
05/14/2024	77	Notice of Request by Pro Hac Vice Melissa Hatch O'Donnell, Esq. to receive Notices of Electronic Filings. (Pro Hac Vice fee $ 250 receipt number ANJDC-15366352.) (CONROY, REBEKAH) (Entered: 05/14/2024)

05/14/2024	78	Notice of Request by Pro Hac Vice Robin P. Summer, Esq. to receive Notices of Electronic Filings. (Pro Hac Vice fee $ 250 receipt number ANJDC-15366358.) (CONROY, REBEKAH) (Entered: 05/14/2024)
05/14/2024	79	Notice of Request by Pro Hac Vice Steven Maddox, Esq. to receive Notices of Electronic Filings. (Pro Hac Vice fee $ 250 receipt number ANJDC-15366362.) (CONROY, REBEKAH) (Entered: 05/14/2024)
05/14/2024		Pro Hac Vice counsel, ANDREW P. ZAPPIA, BRETT GARRISON, JEREMY J. EDWARDS, MELISSA HATCH O'DONNELL, ROBIN P. SUMNER and STEVEN A. MADDOX, has been added to receive Notices of Electronic Filing. Pursuant to L.Civ.R. 101.1, only local counsel are entitled to sign and file papers, enter appearances and receive payments on judgments, decrees or orders. (jd,) (Entered: 05/14/2024)
05/16/2024	80	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. re 68 Order. (WALSH, LIZA) (Entered: 05/16/2024)
05/17/2024	81	LETTER ORDER granting 80 Plaintiff's request to Amend pretrial schedule. Signed by Magistrate Judge Michael A. Hammer on 5/16/2024. (jd,) (Entered: 05/17/2024)
05/22/2024	82	Minute Entry for proceedings held before Judge Stanley R. Chesler: Motion Hearing held on 5/22/2024 re 41 MOTION for Judgment on the Pleadings *as to Counterclaims 1-5* filed by AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS INC., AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, 26 MOTION to Dismiss *DEFENDANTS' COUNTERCLAIM COUNTS 1-10* filed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., TEVA PHARMACEUTICALS USA, INC., Motions Taken Under Advisement: DECISION RESERVED (Court Reporter, Mary Jo Monteleone (973-645-3833)) (tt,) (Entered: 05/22/2024)
05/23/2024	83	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J.. (WALSH, LIZA) (Entered: 05/23/2024)
05/23/2024	85	LETTER ORDER granting 83 Plaintiff's request for a one-week extension of the deadline for the parties to negotiate their ESI protocol, until 5/31/2024. Signed by Magistrate Judge Michael A. Hammer on 5/23/2024. (jd,) (Entered: 05/24/2024)
05/24/2024	84	Transcript of Motion Hearing held on May 22, 2024, before Judge Stanley R. Chesler. Court Reporter: Mary Jo Monteleone (973-645-3833). **NOTICE REGARDING (1) REDACTION OF PERSONAL IDENTIFIERS IN TRANSCRIPTS AND (2) MOTION TO REDACT AND SEAL:** The parties have seven (7) calendar days to file with the Court a Notice of Intent to Request Redaction of this Transcript to comply with Fed.R.Civ.P.5.2(a) (personal identifiers). Parties seeking to redact and seal this Transcript, or portions thereof, pursuant to L.Civ.R. 5.3(g) must e-file a Motion to Redact and Seal utilizing the event `Redact and Seal Transcript/Digital Recording`. Redaction Request to Court Reporter due, but not filed, by 6/14/2024. Redacted Transcript Deadline set for 6/24/2024. Release of Transcript Restriction set for 8/22/2024. (adc) (Entered: 05/24/2024)
05/31/2024	86	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J.. (Attachments: # 1 Text of Proposed Order)(WALSH, LIZA) (Entered: 05/31/2024)
06/03/2024	87	STIPULATION AND ORDER Establishing the protocol for the production of documents and electronically stored information. Signed by Magistrate Judge Michael A. Hammer on 6/3/2024. (jd,) (Entered: 06/03/2024)
06/10/2024	88	OPINION & ORDER denying 26 Plaintiff's Motion to Dismiss Counterclaim Counts 1-10; granting 41 Defendant's Motion for Partial Judgment on the Pleadings. Judgment is entered in favor of Counts 1-5 of Defendants' Counterclaims. Signed by Judge Stanley R. Chesler on 6/10/2024. (jd,) (Entered: 06/10/2024)
06/11/2024	89	TEXT ORDER: The Court having been informed that Teva intends to file a motion to stay, it is ORDERED that: 1) Teva shall file its moving papers by close of business today, June 11, 2024; 2) Amneal shall file its opposition papers by close of business tomorrow, June 12, 2024; and 3) oral argument on the motion shall be heard on Thursday, June 13, 2024 at 11:00 a.m. (re: O/O (d.e. 88)). So Ordered by Judge Stanley R. Chesler on 6/11/2024. (tt,) (Entered: 06/11/2024)
06/11/2024		Set/Reset Hearings: Hearing set for 6/13/2024 at 11:00 AM in Newark - Courtroom 2 before Judge Stanley R. Chesler. regarding ENTRY ((d.e. 89)). ORDERED ALL PARTIES TO APPEAR IN

		PERSON. (tt,) (Entered: 06/11/2024)
06/11/2024	90	MOTION to Stay by All Plaintiffs. (Attachments: # 1 Text of Proposed Order, # 2 Certificate of Service)(WALSH, LIZA) Modified on 6/14/2024 (jd,). (Entered: 06/11/2024)
06/11/2024	91	DECLARATION of Liza M. Walsh re 90 MOTION to Stay by All Plaintiffs. (Attachments: # 1 Brief Memorandum of Law in Support of Motion to Stay, # 2 Exhibit A, # 3 Exhibit B, # 4 Exhibit C) (WALSH, LIZA) NOTICE TO COUNSEL: Counsel is advised that pursuant to Local Civil Rule 5.3(c)(2), a single, consolidated motion to seal shall be filed within 14 days following the completed briefing of the materials sought to be sealed, or within 14 days following the date on which the last of such materials was filed under temporary seal if the motion is resolved, unless otherwise directed by the Court. (Entered: 06/11/2024)
06/11/2024	92	NOTICE OF APPEAL to Federal Circuit as to 88 Order on Motion to Dismiss,, Order on Motion for Judgment on the Pleadings, by NORTON (WATERFORD) LTD., TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., TEVA PHARMACEUTICALS USA, INC.. Filing fee $ 605, receipt number ANJDC-15439392. The Clerk's Office hereby certifies the record and the docket sheet available through ECF to be the certified list in lieu of the record and/or the certified copy of the docket entries. (WALSH, LIZA) (Entered: 06/11/2024)
06/12/2024	93	NOTICE of Appearance by SHALOM D STONE on behalf of AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC (STONE, SHALOM) (Entered: 06/12/2024)
06/12/2024	94	BRIEF in Opposition filed by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC re 90 MOTION to Stay *(Filed Under Seal)* (CONROY, REBEKAH) NOTICE TO COUNSEL: Counsel is advised that pursuant to Local Civil Rule 5.3(c)(2), a single, consolidated motion to seal shall be filed within 14 days following the completed briefing of the materials sought to be sealed, or within 14 days following the date on which the last of such materials was filed under temporary seal if the motion is resolved, unless otherwise directed by the Court. (Entered: 06/12/2024)
06/12/2024	95	DECLARATION of Rebekah Conroy re 94 Brief in Opposition to Motion,, by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (Attachments: # 1 Exhibit Exhibit 1 to Conroy Decl., # 2 Exhibit Exhibit 2 to Conroy Decl.)(CONROY, REBEKAH) (Entered: 06/12/2024)
06/12/2024	99	USCA Case Number 24-1936 for 92 Notice of Appeal (Federal Circuit), filed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., TEVA PHARMACEUTICALS USA, INC.. (Document Restricted - Court Only) (adc,) (Entered: 06/17/2024)
06/13/2024	96	Minute Entry for proceedings held before Judge Stanley R. Chesler: Motion Hearing held on 6/13/2024 re 90 MOTION to Stay filed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., TEVA PHARMACEUTICALS USA, INC. Ordered motion granted for a period of 30 days from this date. OTBSCounsel shall agree on a briefing schedule and submit those dates to the Court. (Court Reporter, Laurie Engemann (973-776-7714)) (tt,) (Entered: 06/13/2024)
06/13/2024	97	Letter from Liza M. Walsh to the Hon. Stanley R. Chesler, U.S.D.J.. (Attachments: # 1 Text of Proposed Order)(WALSH, LIZA) (Entered: 06/13/2024)
06/13/2024	98	ORDER granting in part 97 Plaintiff's Motion to Stay for thirty (30) days to permit resolution of an application to the United States Court of Appeals for the Federal Circuit. Staying the 88 Injunction Order for a period of thirty (30) days, and shall expire on 7/15/2024. The Parties shall meet and confer and propose to the Federal Circuit a briefing schedule for Teva's application for a stay and a briefing schedule for the appeal. Signed by Judge Stanley R. Chesler on 6/13/2024. (jd,) Modified on 6/14/2024 (jd,). (Entered: 06/14/2024)
06/20/2024	100	ORDER of USCA as to 92 Notice of Appeal (Federal Circuit), filed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., TEVA PHARMACEUTICALS USA, INC. (adc,) (Entered: 06/21/2024)
06/21/2024	101	Letter from Liza M. Walsh to the Hon. Michael A. Hammer, U.S.M.J. re 12 Answer to Amended Complaint,,,, Counterclaim,,, 15 Order, 25 Order,,,,,,,. (WALSH, LIZA) (Entered: 06/21/2024)

06/24/2024	102	LETTER ORDER granting 101 Plaintiff Teva's Request for an extension of time from 6/24/2024 to 7/15/2024 for Teva to answer Defendants' Counterclaims (D.E. 12). Signed by Magistrate Judge Michael A. Hammer on 6/24/2024. (dam) (Entered: 06/24/2024)
06/24/2024	103	LETTER ORDER granting the parties' request for an extension from 6/24/2024 until 7/15/2024 for Teva to answer Defendants' Counterclaim. Signed by Magistrate Judge Michael A. Hammer on 6/24/2024. (sm) (Entered: 06/24/2024)
06/26/2024	104	REDACTION to 94 Brief in Opposition to Motion,, *Redacted Defendants' Memorandum of Law* by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (CONROY, REBEKAH) (Entered: 06/26/2024)
06/26/2024	105	REDACTION *Redacted Plaintiffs' Memorandum of Law* by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (Attachments: # 1 Certification Redacted Certification of Liza Walsh)(CONROY, REBEKAH) (Entered: 06/26/2024)
06/26/2024	106	MOTION to Seal *a Portion of the Record* by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (Attachments: # 1 Certification of Rebekah Conroy in Support of Motion to Seal a Portion of the Record, # 2 Index of Confidential Information to be Sealed, # 3 Text of Proposed Order Sealing a Portion of the Record)(CONROY, REBEKAH) (Entered: 06/26/2024)
06/26/2024		CLERK'S QUALITY CONTROL MESSAGE - The LETTER ORDER 103 submitted by the Clerk's Office on 6/24/2024 is a duplicate of 102 . These submissions will remain on the docket unless otherwise ordered by the court. This message is for informational purposes only. (sm) (Entered: 06/26/2024)
06/28/2024		CLERK'S QUALITY CONTROL MESSAGE - Please be advised the Redacted 104 Brief and 105 Plaintiff's memorandum of law submitted by REBEKAH CONROY on 6/26/2024, appears to be designated as sealed/confidential materials. Upon further review of the submissions the documents appear to not have any redactions. The Clerk's Office has restricted access to this document, pending further clarification. (jd,) Modified on 6/28/2024 (jd,). (Entered: 06/28/2024)
06/28/2024		Set Deadlines as to 106 MOTION to Seal a Portion of the Record. Motion set for 8/5/2024 before Magistrate Judge Michael A. Hammer. Unless otherwise directed by the Court, this motion will be decided on the papers and no appearances are required. Note that this is an automatically generated message from the Clerk`s Office and does not supersede any previous or subsequent orders from the Court. (jd,) (Entered: 06/28/2024)
06/28/2024	107	ORDER of USCA as to 92 Notice of Appeal (Federal Circuit), filed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., TEVA PHARMACEUTICALS USA, INC. (adc,) (Entered: 06/28/2024)
07/01/2024	108	REDACTION to 94 Brief in Opposition to Motion,, 104 Redacted Document *Redacted Memorandum of Law* by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (CONROY, REBEKAH) (Entered: 07/01/2024)
07/01/2024	109	REDACTION to 91 Declaration,, *Redacted Plaintiffs' Memorandum of Law* by AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS INC., AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC. (Attachments: # 1 Redacted Certification of Liza Walsh)(CONROY, REBEKAH) (Entered: 07/01/2024)
07/01/2024	110	ORDER of USCA as to 92 Notice of Appeal (Federal Circuit), filed by TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., TEVA PHARMACEUTICALS USA, INC. (adc,) (Entered: 07/02/2024)
07/10/2024	111	Letter from Liza M. Walsh to the Hon. Stanley R. Chesler, U.S.D.J. encl. Joint Claim Construction and Prehearing Statement. (Attachments: # 1 Joint Claim Construction and Prehearing Statement)(WALSH, LIZA) (Entered: 07/10/2024)

PACER Service Center			
Transaction Receipt			
07/15/2024 07:12:02			
PACER Login:	gailrosner	**Client Code:**	103069/391157
Description:	Docket Report	**Search Criteria:**	2:23-cv-20964-SRC-MAH Start date: 1/1/1980 End date: 7/15/2024
Billable Pages:	16	**Cost:**	1.60

Liza M. Walsh
Selina M. Ellis
WALSH PIZZI O'REILLY FALANGA LLP
Three Gateway Center
100 Mulberry Street, 15th Floor
Newark, New Jersey 07102
Tel: (973) 757-1100

Attorneys for Plaintiffs Teva Branded Pharmaceutical Products R&D, Inc., Norton (Waterford) Ltd., and Teva Pharmaceuticals USA, Inc.

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., and TEVA PHARMACEUTICALS USA, INC. Plaintiffs, v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS LLC, and AMNEAL PHARMACEUTICALS INC. Defendants.	Civil Action No. 23-cv-20964-JXN-MAH

FIRST AMENDED COMPLAINT

Plaintiffs Teva Branded Pharmaceutical Products R&D, Inc. ("Teva Branded"), Norton (Waterford) Ltd. ("Norton"), and Teva Pharmaceuticals USA, Inc. ("Teva USA") (collectively, "Plaintiffs"), by their undersigned attorneys, for their First Amended Complaint against Defendants Amneal Pharmaceuticals of New York, LLC ("Amneal NY"), Amneal Ireland Limited ("Amneal Ireland"), Amneal Pharmaceuticals LLC ("Amneal Pharma"), and Amneal

Pharmaceuticals Inc. ("Amneal Inc.") (collectively, "Amneal" or "Defendants"), allege as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement under the patent laws of the United States, 35 U.S.C. § 100 *et seq.*, including 35 U.S.C. § 271, the Drug Price Competition and Patent Term Restoration Act of 1984, 21 U.S.C. § 355(j) ("Hatch-Waxman Act"), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, that arises out of Amneal's submission of Abbreviated New Drug Application ("ANDA") No. 211600 to the U.S. Food and Drug Administration ("FDA") seeking approval to commercially manufacture, use, offer for sale, sell, and/or import a generic version of ProAir® HFA (albuterol sulfate) Inhalation Aerosol prior to the expiration of U.S. Patent Nos. 8,132,712 ("the '712 patent"), 9,463,289 ("the '289 patent"), 9,808,587 ("the '587 patent"), 10,561,808 ("the '808 patent"), and 11,395,889 ("the '889 patent"). Collectively, the '712 patent, the '289 patent, the '587 patent, the '808 patent, and the '889 patent are referred to herein as the "Patents-in-Suit."

THE PARTIES

Plaintiffs

2. Plaintiff Teva Branded is a company organized under the laws of the State of Delaware with its principal place of business at 145 Brandywine Parkway, West Chester, Pennsylvania 19380. In addition, Teva Branded has a place of business at 400 Interpace Parkway #3, Parsippany, New Jersey 07054.

3. Plaintiff Norton is a private limited company organized under the laws of the Republic of Ireland and having its registered office at Unit 301, IDA Industrial Park, Waterford X91 WK68, Republic of Ireland. Norton trades, *i.e.*, does business, as Ivax Pharmaceuticals Ireland and as Teva Pharmaceuticals Ireland.

indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.

46. On October 1, 2022, the manufacturing of branded ProAir® HFA (albuterol sulfate) Inhalation Aerosol was discontinued. Teva USA currently distributes an authorized generic of ProAir® HFA (albuterol sulfate) Inhalation Aerosol under NDA No. 021457 in the United States.

The '712 Patent

47. The '712 patent, titled "Metered-Dose Inhaler," duly and legally issued on March 13, 2012. A true and correct copy of the '712 patent is attached hereto as Exhibit A.

48. Norton is the owner and assignee of the '712 patent.

49. The '712 patent is listed in connection with ProAir® HFA (NDA No. 021457) in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book").

50. The Orange Book currently lists the expiration of the '712 patent as September 7, 2028.

The '289 Patent

51. The '289 patent, titled "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof," duly and legally issued on October 11, 2016. A true and correct copy of the '289 patent is attached hereto as Exhibit B.

52. Norton is the owner and assignee of the '289 patent.

53. The '289 patent is listed in connection with ProAir® HFA (NDA No. 021457) in the Orange Book.

54. The Orange Book currently lists the expiration of the '289 patent as May 18, 2031.

The '587 Patent

55. The '587 patent, titled "Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator," duly and legally issued on November 7, 2017. A true and correct copy of the '587 patent is attached hereto as Exhibit C.

56. Norton is the owner and assignee of the '587 patent.

57. The '587 patent is listed in connection with ProAir® HFA (NDA No. 021457) in the Orange Book.

58. The Orange Book currently lists the expiration of the '587 patent as May 18, 2031.

The '808 Patent

59. The '808 patent, titled "Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator," duly and legally issued on February 18, 2020. A true and correct copy of the '808 patent is attached hereto as Exhibit D.

60. Norton is the owner and assignee of the '808 patent.

61. The '808 patent is listed in connection with ProAir® HFA (NDA No. 021457) in the Orange Book.

62. The Orange Book currently lists the expiration of the '808 patent as January 1, 2032.

The ' 889 Patent

63. The '889 patent, titled "Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator," duly and legally issued on July 26, 2022. A true and correct copy of the '889 patent is attached hereto as Exhibit E.

64. Norton is the owner and assignee of the '889 patent.

65. The '889 patent is listed in connection with ProAir® HFA (NDA No. 021457) in the Orange Book.

66. The Orange Book currently lists the expiration of the '889 patent as May 18, 2031.

Defendants' ANDA and Notice of Paragraph IV Certification

67. On information and belief, Defendants have submitted or caused the submission of Amneal's ANDA to FDA under 21 U.S.C. § 355(j), to obtain approval to engage in the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of the Amneal ANDA Products prior to the expiration of the Patents-in-Suit.

68. On information and belief, FDA has not yet approved Amneal's ANDA.

69. In the Amneal Notice Letter, Defendant Amneal NY notified Plaintiffs of the submission of Amneal's ANDA to FDA.

70. In the Amneal Notice Letter, Defendant Amneal NY notified Plaintiffs that Amneal had filed a Paragraph IV Certification with respect to each of the Patents-in-Suit and was seeking approval from FDA to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the Patents-in-Suit.

71. The purpose of Defendants' submission of Amneal's ANDA to FDA was to obtain approval under the Federal Food, Drug and Cosmetic Act to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the Patents-in-Suit.

72. On information and belief, Defendants, through their own actions and through the actions of their agents, affiliates, and subsidiaries, prepared and submitted Amneal's ANDA, and intend to further prosecute Amneal's ANDA. On information and belief, if FDA approves

Amneal's ANDA, Defendants will manufacture, offer for sale, or sell the Amneal ANDA Products within the United States, or will import the Amneal ANDA Products into the United States. On information and belief, if FDA approves Amneal's ANDA, Defendants, through their own actions and through the actions of their agents, affiliates, and subsidiaries, will actively induce or contribute to the manufacture, use, offer for sale, sale, or importation of the Amneal ANDA Products in or into the United States.

73. In the Amneal Notice Letter, Defendant Amneal NY stated that the subject of Amneal's ANDA is "Albuterol Sulfate Inhalation Aerosol, 90 mcg per actuation."

74. In the Amneal Notice Letter, Defendant Amneal NY stated that the active ingredient of the Amneal ANDA Products is albuterol sulfate.

75. In the Amneal Notice Letter, Defendant Amneal NY stated that the dosage form of the Amneal ANDA Products is "inhalation aerosol."

76. In the Amneal Notice Letter, Defendant Amneal NY stated that the strength of the Amneal ANDA Products is 90 mcg per actuation.

77. On information and belief, Amneal's ANDA contains a Paragraph IV Certification with respect to each of the Patents-in-Suit asserting that the Patents-in-Suit are unenforceable, invalid, and/or will not be infringed by the manufacture, use, offer for sale, sale, or importation of the Amneal ANDA Products ("Amneal's Paragraph IV Certification"). Defendants notified Plaintiffs of Amneal's Paragraph IV Certification in the Amneal Notice Letter, dated August 24, 2023, sent by United Parcel Service.

78. In the Amneal Notice Letter, Defendants offered Plaintiffs confidential access to ANDA No. 211600 on terms and conditions set forth in an attached "Offer of Confidential

Access" ("OCA"). The OCA provided by Defendants contained various terms and conditions, several of which went above and beyond protections typically afforded in a protective order.

79. By correspondence, counsel for Plaintiffs and counsel for Defendants discussed the terms of Defendants' OCA.

80. On September 16, 2023, Plaintiffs' counsel sent Defendants' counsel an email identifying various unreasonably restrictive terms in Defendants' OCA. Plaintiffs' counsel also included a revised draft of the OCA in this correspondence.

81. On September 25, 2023, Defendants' counsel sent Plaintiffs' counsel a revised OCA. That offer addressed some of Plaintiffs' concerns but remained unreasonably restrictive.

82. On September 27, 2023, Plaintiffs' counsel sent another email reiterating its concerns regarding the restrictions in Defendants' OCA, and attaching a revised draft of the OCA.

83. On September 28, 2023, the parties reached agreement on the terms of the OCA, which was finalized on October 2, 2023. Amneal did not produce any portion of its ANDA until October 3, 2023 and did not produce the requested samples until October 4, 2023, shortly before the 45-day statutory deadline to file suit.

84. The Amneal Notice Letter appends a document titled "Detailed Factual and Legal Basis of Non-Infringement, Unenforceability, and/or Invalidity" asserting that the commercial manufacture, use, offer for sale, or sale of the Amneal ANDA Products will not infringe any of the Patents-in-Suit ("Detailed Statement"). However, the Amneal Notice Letter and "Detailed Statement" do not provide information regarding the Amneal ANDA Products sufficient to evaluate Defendants' assertions of noninfringement.

85. Given the 45-day statutory deadline to file suit set forth in 21 U.S.C. § 355(j)(5)(B)(iii), the timing of the production of Amneal's ANDA and samples, and the limited information provided by Defendants to date, Plaintiffs turn to the judicial process and the aid of discovery to obtain, under appropriate judicial safeguards, such information as is required to further confirm their allegations of infringement and to present to the Court evidence that the Amneal ANDA Products fall within the scope of one or more claims of the Patents-in-Suit.

86. This action was commenced within 45 days from the date of Plaintiffs' receipt of the Amneal Notice Letter.

COUNT I – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 8,132,712 UNDER 35 U.S.C. § 271(e)(2)

87. Plaintiffs incorporate each of the preceding paragraphs 1–86 as if fully set forth herein.

88. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '712 patent was an act of infringement of the '712 patent under 35 U.S.C. § 271(e)(2)(A).

89. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '712 patent under 35 U.S.C. § 271(a)-(c).

90. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '712 patent, including at least claim 1, either literally or under the doctrine of equivalents.

91. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '712 patent.

92. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

93. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '712 patent, including at least claim 1.

94. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '712 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

95. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '712 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '712 patent after approval of Amneal's ANDA.

96. The foregoing actions by Amneal constitute and/or will constitute infringement of the '712 patent, active inducement of infringement of the '712 patent, and contribution to the infringement by others of the '712 patent.

97. On information and belief, Amneal has acted with full knowledge of the '712 patent and without a reasonable basis for believing that it would not be liable for infringing the '712 patent, actively inducing infringement of the '712 patent, and contributing to the infringement by others of the '712 patent.

98. Unless Amneal is enjoined from infringing the '712 patent, actively inducing infringement of the '712 patent, and contributing to the infringement by others of the '712 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT II – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 8,132,712

99. Plaintiffs incorporate each of the preceding paragraphs 1–98 as if fully set forth herein.

100. Amneal has knowledge of the '712 patent.

101. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '712 patent, including at least claim 1, either literally or under the doctrine of equivalents.

102. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

103. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '712 patent, including at least claim 1.

104. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '712 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

105. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '712 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-

infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '712 patent after approval of Amneal's ANDA.

106. The foregoing actions by Amneal constitute and/or will constitute infringement of the '712 patent, active inducement of infringement of the '712 patent, and contribution to the infringement by others of the '712 patent.

107. On information and belief, Amneal has acted with full knowledge of the '712 patent and without a reasonable basis for believing that it would not be liable for infringing the '712 patent, actively inducing infringement of the '712 patent, and contributing to the infringement by others of the '712 patent.

108. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '712 patent, including at least claim 1, and whether said claims of the '712 patent are valid.

109. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '712 patent and that the claims of the '712 patent are valid.

110. Amneal should be enjoined from infringing the '712 patent, actively inducing infringement of the '712 patent, and contributing to the infringement by others of the '712 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT III – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 9,463,289 UNDER 35 U.S.C. § 271(e)(2)

111. Plaintiffs incorporate each of the preceding paragraphs 1–110 as if fully set forth herein.

112. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '289 patent was an act of infringement of the '289 patent under 35 U.S.C. § 271(e)(2)(A).

113. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '289 patent under 35 U.S.C. § 271(a)-(c).

114. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '289 patent, including at least claim 1, either literally or under the doctrine of equivalents.

115. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '289 patent.

116. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

117. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '289 patent, including at least claim 1.

118. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '289 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

119. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '289 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '289 patent after approval of Amneal's ANDA.

120. The foregoing actions by Amneal constitute and/or will constitute infringement of the '289 patent, active inducement of infringement of the '289 patent, and contribution to the infringement by others of the '289 patent.

121. On information and belief, Amneal has acted with full knowledge of the '289 patent and without a reasonable basis for believing that it would not be liable for infringing the '289 patent, actively inducing infringement of the '289 patent, and contributing to the infringement by others of the '289 patent.

122. Unless Amneal is enjoined from infringing the '289 patent, actively inducing infringement of the '289 patent, and contributing to the infringement by others of the '289 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT IV – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 9,463,289

123. Plaintiffs incorporate each of the preceding paragraphs 1–122 as if fully set forth herein.

124. Amneal has knowledge of the '289 patent.

125. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '289 patent, including at least claim 1, either literally or under the doctrine of equivalents.

126. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

127. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '289 patent, including at least claim 1.

128. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '289 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

129. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '289 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '289 patent after approval of Amneal's ANDA.

130. The foregoing actions by Amneal constitute and/or will constitute infringement of the '289 patent, active inducement of infringement of the '289 patent, and contribution to the infringement by others of the '289 patent.

131. On information and belief, Amneal has acted with full knowledge of the '289 patent and without a reasonable basis for believing that it would not be liable for infringing the

'289 patent, actively inducing infringement of the '289 patent, and contributing to the infringement by others of the '289 patent.

132. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '289 patent, including at least claim 1, and whether said claims of the '289 patent are valid.

133. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '289 patent and that the claims of the '289 patent are valid.

134. Amneal should be enjoined from infringing the '289 patent, actively inducing infringement of the '289 patent, and contributing to the infringement by others of the '289 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT V – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 9,808,587 UNDER 35 U.S.C. § 271(e)(2)

135. Plaintiffs incorporate each of the preceding paragraphs 1–134 as if fully set forth herein.

136. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '587 patent was an act of infringement of the '587 patent under 35 U.S.C. § 271(e)(2)(A).

137. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '587 patent under 35 U.S.C. § 271(a)-(c).

138. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '587 patent, including at least claim 1, either literally or under the doctrine of equivalents.

139. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '587 patent.

140. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

141. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '587 patent, including at least claim 1.

142. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '587 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

143. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '587 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-

infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '587 patent after approval of Amneal's ANDA.

144. The foregoing actions by Amneal constitute and/or will constitute infringement of the '587 patent, active inducement of infringement of the '587 patent, and contribution to the infringement by others of the '587 patent.

145. On information and belief, Amneal has acted with full knowledge of the '587 patent and without a reasonable basis for believing that it would not be liable for infringing the '587 patent, actively inducing infringement of the '587 patent, and contributing to the infringement by others of the '587 patent.

146. Unless Amneal is enjoined from infringing the '587 patent, actively inducing infringement of the '587 patent, and contributing to the infringement by others of the '587 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VI – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 9,808,587

147. Plaintiffs incorporate each of the preceding paragraphs 1–146 as if fully set forth herein.

148. Amneal has knowledge of the '587 patent.

149. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '587 patent, including at least claim 1, either literally or under the doctrine of equivalents.

150. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

151. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '587 patent, including at least claim 1.

152. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '587 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

153. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '587 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '587 patent after approval of Amneal's ANDA.

154. The foregoing actions by Amneal constitute and/or will constitute infringement of the '587 patent, active inducement of infringement of the '587 patent, and contribution to the infringement by others of the '587 patent.

155. On information and belief, Amneal has acted with full knowledge of the '587 patent and without a reasonable basis for believing that it would not be liable for infringing the '587 patent, actively inducing infringement of the '587 patent, and contributing to the infringement by others of the '587 patent.

156. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '587 patent, including at least claim 1, and whether said claims of the '587 patent are valid.

157. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '587 patent and that the claims of the '587 patent are valid.

158. Amneal should be enjoined from infringing the '587 patent, actively inducing infringement of the '587 patent, and contributing to the infringement by others of the '587 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VII – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 10,561,808 UNDER 35 U.S.C. § 271(e)(2)

159. Plaintiffs incorporate each of the preceding paragraphs 1–158 as if fully set forth herein.

160. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '808 patent was an act of infringement of the '808 patent under 35 U.S.C. § 271(e)(2)(A).

161. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '808 patent under 35 U.S.C. § 271(a)-(c).

162. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '808 patent, including at least claim 1, either literally or under the doctrine of equivalents.

163. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '808 patent.

164. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

165. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '808 patent, including at least claim 1.

166. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '808 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

167. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '808 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '808 patent after approval of Amneal's ANDA.

168. The foregoing actions by Amneal constitute and/or will constitute infringement of the '808 patent, active inducement of infringement of the '808 patent, and contribution to the infringement by others of the '808 patent.

169. On information and belief, Amneal has acted with full knowledge of the '808 patent and without a reasonable basis for believing that it would not be liable for infringing the '808 patent, actively inducing infringement of the '808 patent, and contributing to the infringement by others of the '808 patent.

170. Unless Amneal is enjoined from infringing the '808 patent, actively inducing infringement of the '808 patent, and contributing to the infringement by others of the '808 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT VIII – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 10,561,808

171. Plaintiffs incorporate each of the preceding paragraphs 1–170 as if fully set forth herein.

172. Amneal has knowledge of the '808 patent.

173. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '808 patent, including at least claim 1, either literally or under the doctrine of equivalents.

174. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

175. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '808 patent, including at least claim 1.

176. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '808 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

177. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '808 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-

infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '808 patent after approval of Amneal's ANDA.

178. The foregoing actions by Amneal constitute and/or will constitute infringement of the '808 patent, active inducement of infringement of the '808 patent, and contribution to the infringement by others of the '808 patent.

179. On information and belief, Amneal has acted with full knowledge of the '808 patent and without a reasonable basis for believing that it would not be liable for infringing the '808 patent, actively inducing infringement of the '808 patent, and contributing to the infringement by others of the '808 patent.

180. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '808 patent, including at least claim 1, and whether said claims of the '808 patent are valid.

181. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '808 patent and that the claims of the '808 patent are valid.

182. Amneal should be enjoined from infringing the '808 patent, actively inducing infringement of the '808 patent, and contributing to the infringement by others of the '808 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT IX – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 11,395,889 UNDER 35 U.S.C. § 271(e)(2)

183. Plaintiffs incorporate each of the preceding paragraphs 1–182 as if fully set forth herein.

184. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '889 patent was an act of infringement of the '889 patent under 35 U.S.C. § 271(e)(2)(A).

185. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '889 patent under 35 U.S.C. § 271(a)-(c).

186. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '889 patent, including at least claim 1, either literally or under the doctrine of equivalents.

187. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '889 patent.

188. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

189. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '889 patent, including at least claim 1.

190. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '889 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

191. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '889 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '889 patent after approval of Amneal's ANDA.

192. The foregoing actions by Amneal constitute and/or will constitute infringement of the '889 patent, active inducement of infringement of the '889 patent, and contribution to the infringement by others of the '889 patent.

193. On information and belief, Amneal has acted with full knowledge of the '889 patent and without a reasonable basis for believing that it would not be liable for infringing the '889 patent, actively inducing infringement of the '889 patent, and contributing to the infringement by others of the '889 patent.

194. Unless Amneal is enjoined from infringing the '889 patent, actively inducing infringement of the '889 patent, and contributing to the infringement by others of the '889 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

COUNT X – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 11,395,889

195. Plaintiffs incorporate each of the preceding paragraphs 1–194 as if fully set forth herein.

196. Amneal has knowledge of the '889 patent.

197. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '889 patent, including at least claim 1, either literally or under the doctrine of equivalents.

198. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

199. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '889 patent, including at least claim 1.

200. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '889 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

201. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '889 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '889 patent after approval of Amneal's ANDA.

202. The foregoing actions by Amneal constitute and/or will constitute infringement of the '889 patent, active inducement of infringement of the '889 patent, and contribution to the infringement by others of the '889 patent.

203. On information and belief, Amneal has acted with full knowledge of the '889 patent and without a reasonable basis for believing that it would not be liable for infringing the

'889 patent, actively inducing infringement of the '889 patent, and contributing to the infringement by others of the '889 patent.

204. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '889 patent, including at least claim 1, and whether said claims of the '889 patent are valid.

205. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '889 patent and that the claims of the '889 patent are valid.

206. Amneal should be enjoined from infringing the '889 patent, actively inducing infringement of the '889 patent, and contributing to the infringement by others of the '889 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request the following relief:

(a) A judgment that each of the Patents-in-Suit has been infringed under 35 U.S.C. § 271(e)(2) by Defendants' submission to FDA of Amneal's ANDA;

(b) A judgment that the Patents-in-Suit are valid and enforceable;

(c) A judgment pursuant to, among other things, 35 U.S.C. § 271(e)(4)(A) ordering that the effective date of any FDA approval for Defendants to make, use, offer for sale, sell, market, distribute, or import the Amneal ANDA Products, or any other product, the making, using, offering for sale, sale, marketing, distribution, or importation of which infringes the

Exhibit A

US008132712B2

(12) **United States Patent**
Fenlon

(10) **Patent No.: US 8,132,712 B2**
(45) **Date of Patent: Mar. 13, 2012**

(54) **METERED-DOSE INHALER**

(75) Inventor: **Derek Fenlon**, Waterford (IE)

(73) Assignee: **Ivax Pharmaceuticals Ireland**, Waterford (IE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 159 days.

(21) Appl. No.: **12/532,762**

(22) PCT Filed: **Apr. 1, 2008**

(86) PCT No.: **PCT/EP2008/002590**

§ 371 (c)(1),
(2), (4) Date: **Sep. 23, 2009**

(87) PCT Pub. No.: **WO2008/119552**

PCT Pub. Date: **Oct. 9, 2008**

(65) **Prior Publication Data**

US 2010/0078490 A1 Apr. 1, 2010

Related U.S. Application Data

(60) Provisional application No. 60/921,320, filed on Apr. 2, 2007.

(30) **Foreign Application Priority Data**

Apr. 11, 2007 (GB) 076999.0

(51) **Int. Cl.**
G06M 1/04 (2006.01)
A61M 11/00 (2006.01)

(52) **U.S. Cl.** ..... **235/91 R**; 128/200.23

(58) **Field of Classification Search** 235/91; 128/200.23
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,445,404	A *	5/1984	Parker	81/62
5,485,971	A *	1/1996	Nakaya et al.	242/381.1
5,489,143	A *	2/1996	Adachi et al.	297/411.38
5,490,749	A *	2/1996	Arbues	410/103
5,794,978	A *	8/1998	Nishide	280/806
6,070,502	A *	6/2000	Chang	81/63
6,175,994	B1 *	1/2001	Nicoletti	24/68 SK
6,267,315	B1 *	7/2001	Blackadder et al.	242/384
6,446,627	B1 *	9/2002	Bowman et al.	128/200.23
7,252,065	B1 *	8/2007	Keeton	123/185.14
2011/0220450	A1 *	9/2011	Chiang	192/64

FOREIGN PATENT DOCUMENTS

WO	WO 98/28033 A	7/1998
WO	WO 2005/114563 A	12/2005

OTHER PUBLICATIONS

International Search Report dated Jul. 10, 2008, application No. PCT/EP2008/002590.

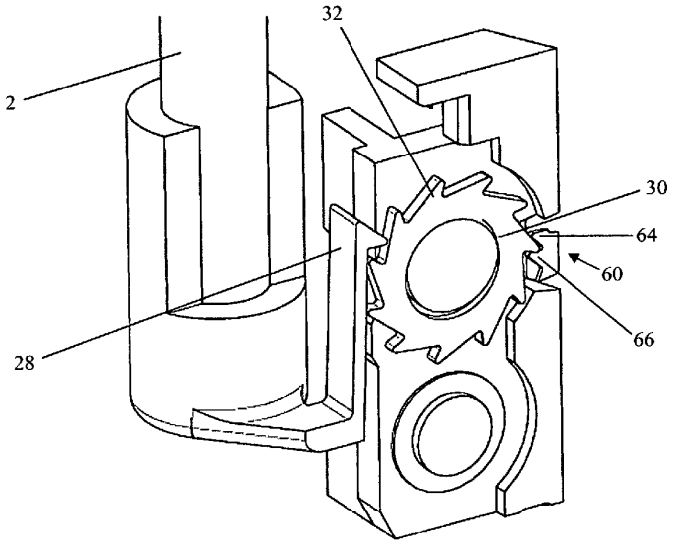
* cited by examiner

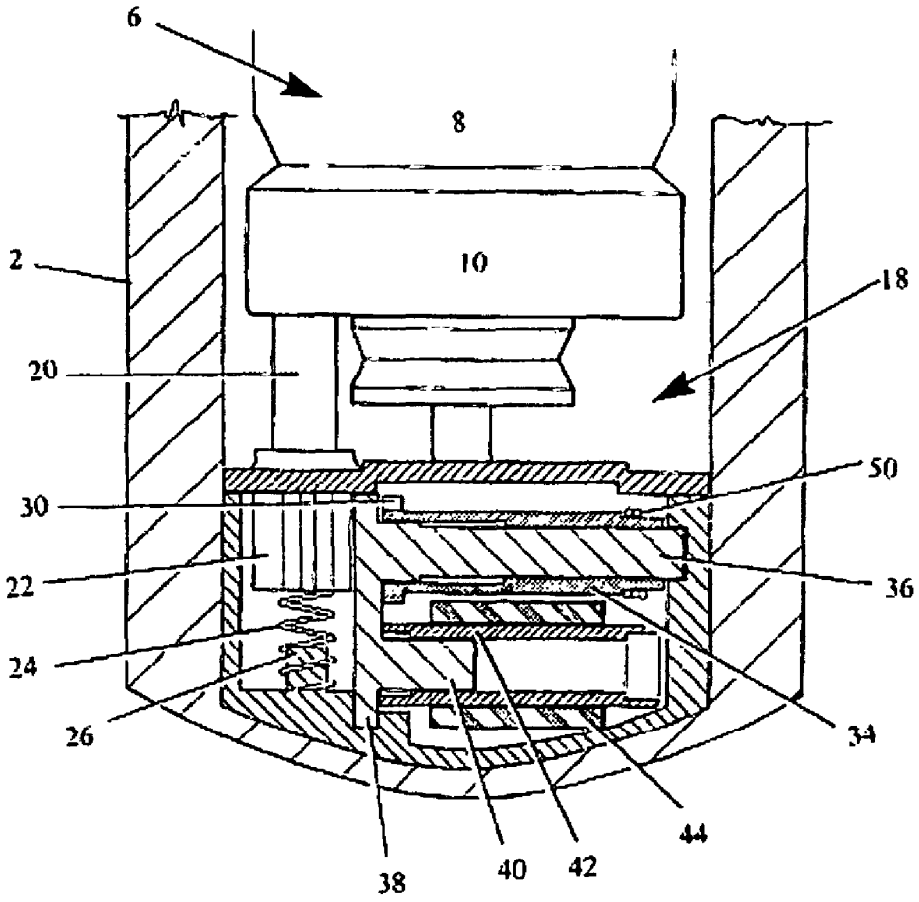
Primary Examiner — Daniel Hess
(74) *Attorney, Agent, or Firm* — RatnerPrestia

(57) **ABSTRACT**

A metered dose inhaler dose counter, the counter includes: an actuator; a rotary gear wheel having a plurality of ratchet teeth; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator; a pawl that prevents reverse rotation of the rotary gear; and a display coupled to the rotary gear.

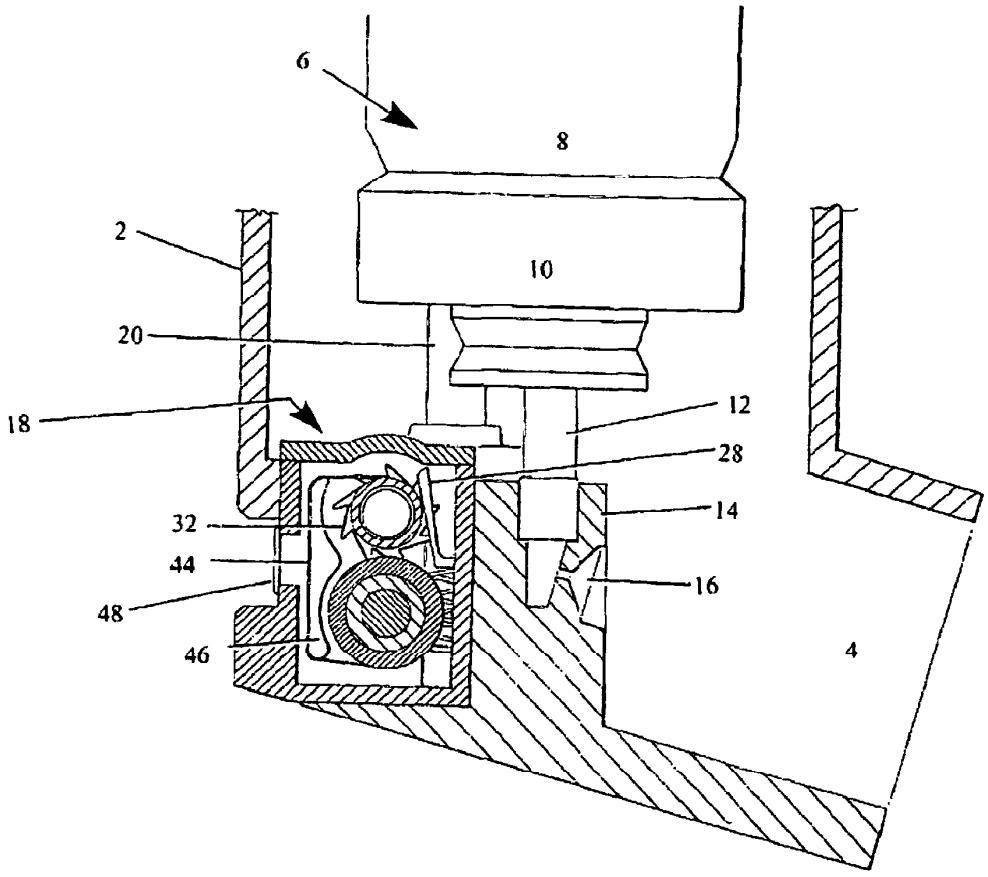
19 Claims, 8 Drawing Sheets





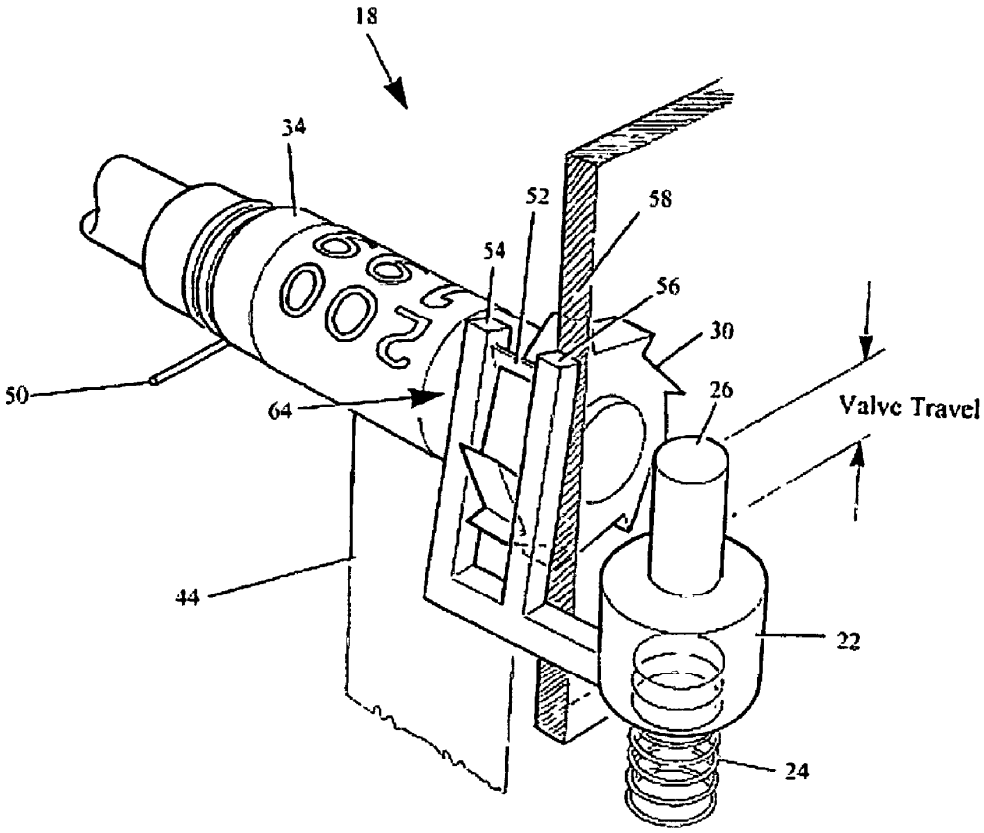
(Prior art)

Fig. 1



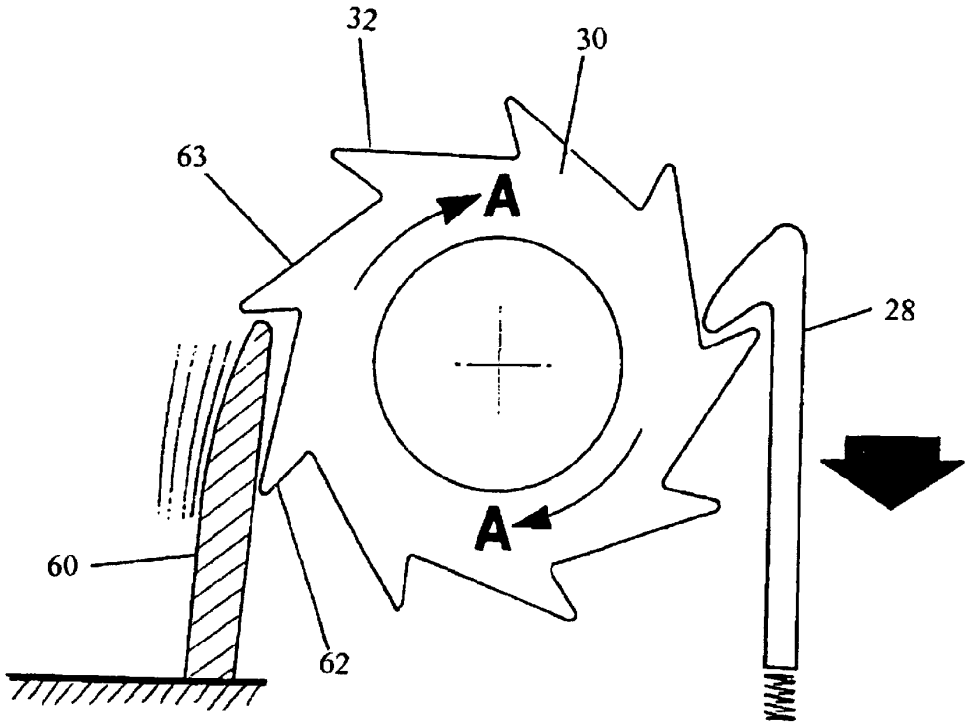
(Prior art)

Fig. 2



(Prior art)

Fig. 3



(Prior art)

Fig. 4

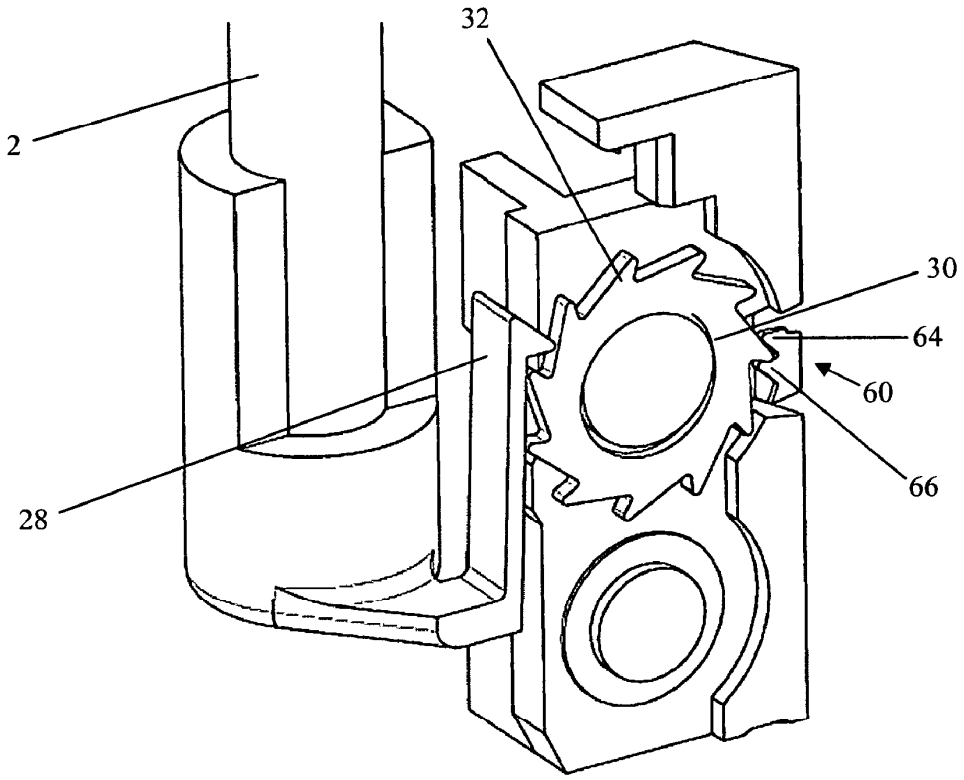


Fig. 5

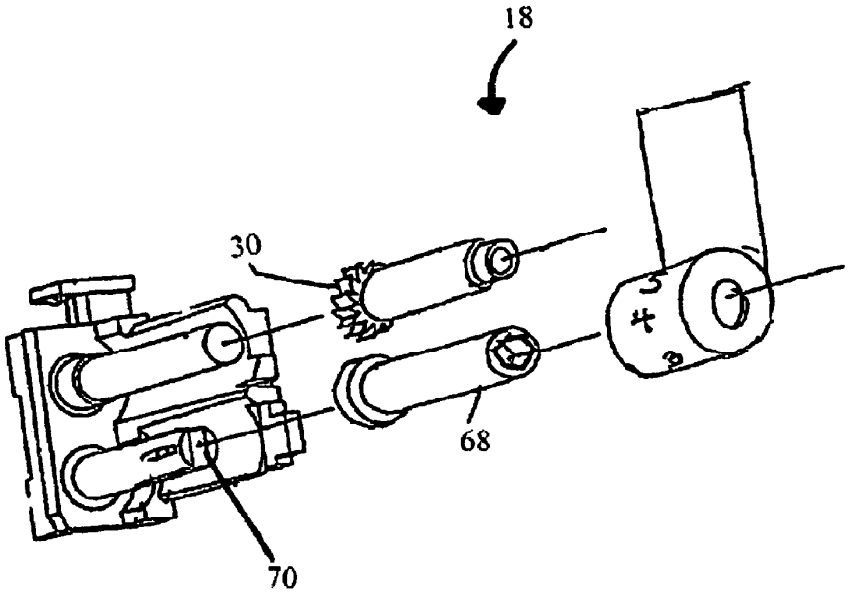

18
30
68
70

Fig. 6

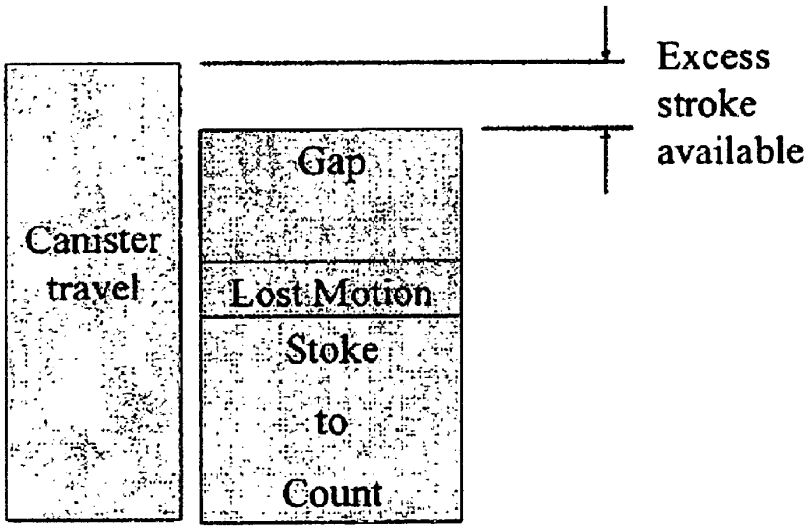

Excess
stroke
available
Gap
Canister
travel
Lost Motion
Stoke
to
Count

Fig. 7

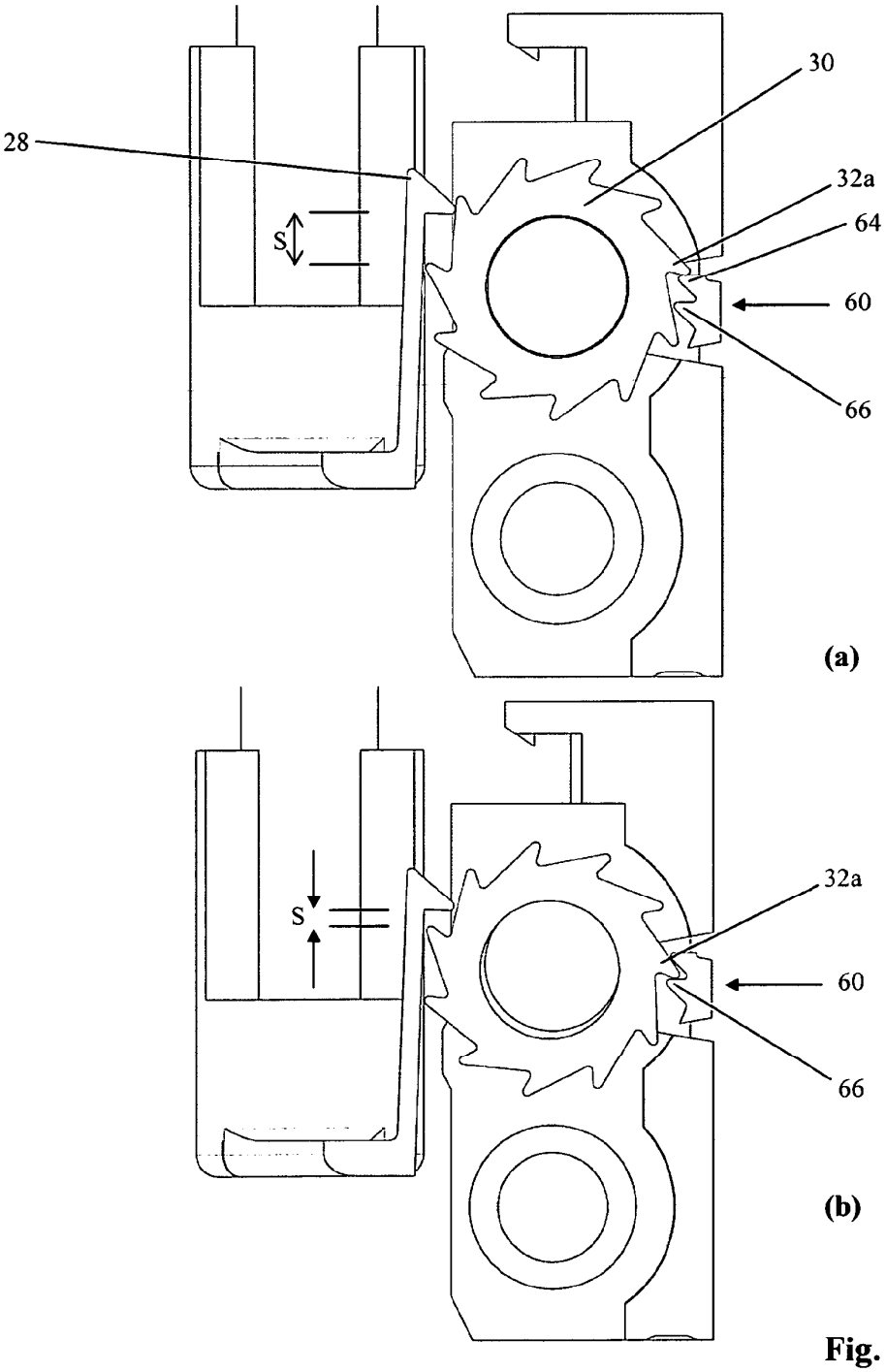


Fig. 8

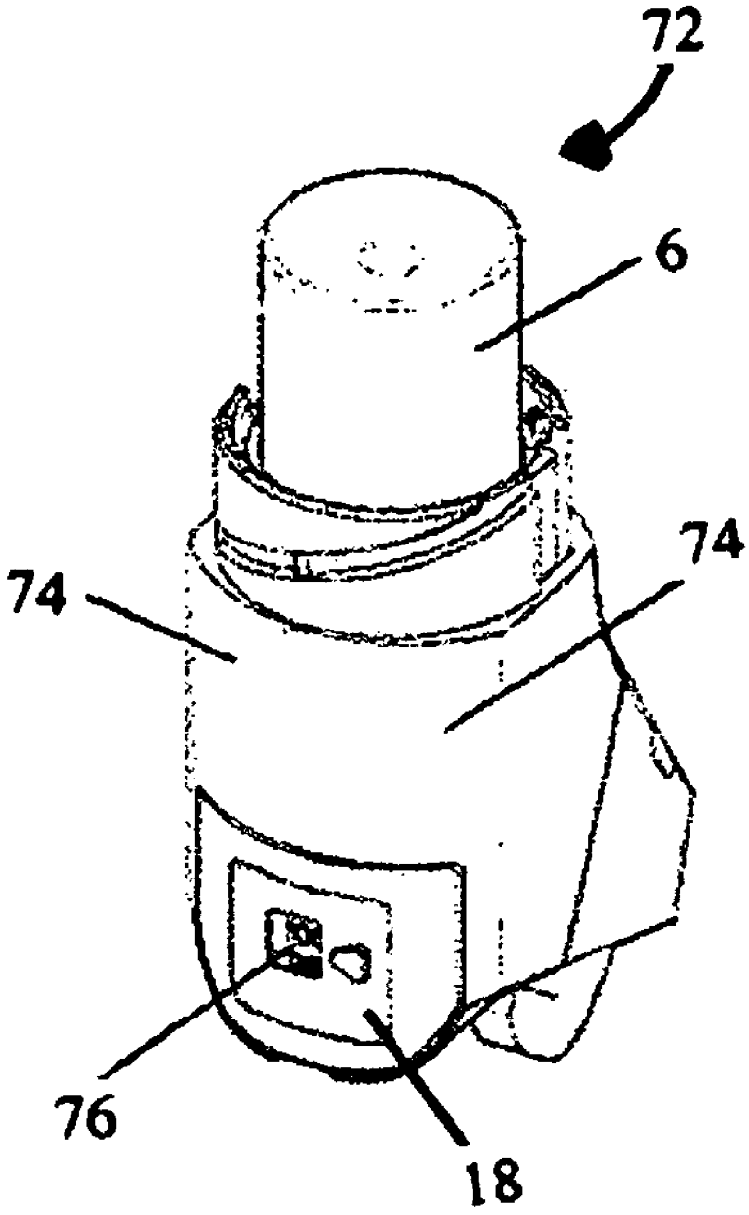


Fig. 9

METERED-DOSE INHALER

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is the U.S. national phase application of PCT International Application No. PCT/EP2008/002590, filed Apr. 1, 2008, which claims priority to U.S. Provisional Patent Application No. 60/921,320, filed Apr. 2, 2007, and GB Application No. 0706999.0, filed Apr. 11, 2007, the contents of such applications being incorporated by reference herein.

FIELD OF THE INVENTION

This invention relates to a metered-dose inhaler and in particular to a dose counter for a metered-dose inhaler, the counter comprising: an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery; a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear; wherein the pawl comprises at least two ratchet teeth which are radially spaced such that one of the teeth engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

BACKGROUND OF THE INVENTION

Metered-dose inhalers include pressurised metered-dose inhalers (of both manually operable and breath-actuated types) and dry-powder inhalers. Such metered-dose inhalers typically comprise a medicament-containing vessel and an actuator body having a drug delivery outlet.

The medicament-containing vessel may be a pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-drawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use, is inserted as a tight push fit into a so-called "stem block" in the actuator body.

To actuate the conventional manually operable inhaler, the user applies a compressive force to the closed end of the canister. The internal components of the metering valve assembly are spring loaded so that a compressive force of about 15 to 30 N is required to activate the device.

In response to this compressive force, the canister moves axially with respect to the valve stem by an amount varying from about 2 to 4 mm. This degree of axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and propellant to be expelled through the valve stem. This is then released into the mouthpiece via a nozzle in the stem block. A user inhaling through the drug delivery outlet of the device at this point will thus receive a dose of the drug.

Metered-dose inhalers as described above administer an accurate dose of medicament whenever required, which is particularly useful for users whose respiratory difficulties manifest themselves suddenly. Such has been the success of these devices that they are now used throughout the world.

A more recent development is the so-called "breath-operated actuator" which delivers a dose of drug through a mouthpiece in response to inhalation by the user. This type of arrangement is particularly convenient in circumstances where the co-ordination between user inhalation and manual depression of the aerosol canister is imperfect. For example, children sometimes lack the necessary co-ordination to achieve effective self-administration and, at times of respiratory distress, adult users may also experience poor co-ordination.

SUMMARY OF THE INVENTION

One of the drawbacks of self-administration from an inhaler is that users often experience difficulty in determining when the charge in the medicament-containing vessel has nearly run out since the contents of the medicament reservoir are typically invisible to the user. With aerosol canisters, part of the reason for this difficulty is that a surplus of propellant may remain in the canister even though the drug supply is nearly exhausted. Alternatively, the near-exhausted state may result in a surplus of drug in relation to propellant. Thus, the illusion is created that the inhaler is still capable of providing useful doses of medicament simply because the canister contains liquid. This is potentially hazardous for the user since dosing becomes unreliable and because few users routinely carry a back-up device.

Many users have several different inhalers for the treatment of a variety of conditions. Others keep inhalers at a number of different locations such as at school, home, work etc. In these circumstances it is particularly difficult for the user to keep track of the amount of usage extracted from each individual inhaler apparatus.

Clearly there is a need for a counter mechanism which enables users to assess how many doses remain in the obscured canister. Such a counter would ensure that users are warned when the inhaler nears exhaustion so that appropriate measures can be taken to avoid running out of medication. Moreover, if a dose counter can provide readability to a resolution of one dose, this can be used for compliance monitoring, either under hospital supervision or by parents and teachers assessing compliance by children in their care. In addition, there are regulatory requirements for metered-dose inhalers to have a dose counter in a number of countries.

WO 98/28033 discloses a dose counter suitable for use with the above-described metered-dose inhalers. FIGS. **1** and **2** reproduced herein from WO 98/28033 show the lower portion of a metered-dose inhaler. The inhaler comprises an actuator body **2** having a drug delivery outlet **4**. An aerosol canister **6** extends into the lower portion of the actuator **2**. The aerosol canister **6** is formed from a deep-drawn aluminium cup **8** to which a lid **10** is attached by crimping.

The lid **10** carries a metering-valve assembly having a protruding valve stem **12**, the end of which is received as a tight push fit in a stem block **14** of the actuator body **2**. Stem block **14** has a nozzle **16** communicating with the drug delivery outlet **4** so that, upon actuation of the metering-valve assembly, a charge of the drug is emitted through the nozzle **16** into the drug delivery outlet **4**. Actuation of the metering-valve assembly is effected by causing downward movement of the aerosol canister **6** relative to the actuator body **2**. This may be achieved through manual pressure exerted by the user against the upturned base (not shown) of the aerosol canister **6** or by automatic depression of the aerosol canister **6** in response to user inhalation in inhalers of the breath-actuated type. The mechanism of breath actuation does not form part of WO 98/28033 or the present invention and will not be described in further detail. A user inhaling through the drug

delivery outlet **4** when the aerosol canister **6** is depressed will receive a metered dose of the drug.

A counter mechanism **18** includes an actuator **20** moulded from a plastics material, such as nylon, the actuator **20** having a boss **22** integrally formed at its base.

The underside of boss **22** is formed with a blind hole which receives a compression spring **24** mounted on an upstanding spigot **26** formed on a lower element of the counter chassis.

A driver **28** for driving a rotary gear in the form of a ratchet-toothed wheel **30** is integrally moulded with boss **22** of the actuator **20** and comprises a transverse hook element (not shown) mounted between two arms (only one visible in FIG. **2**), the bases of which are conjoined to the boss **22**. The transverse hook is dimensioned and oriented to engage with ratchet teeth **32** formed around the periphery of the ratchet-toothed wheel **30** to rotate it in a forward direction.

The ratchet-toothed wheel **30** is integrally moulded with a first hollow axle **34** which is rotatably supported on a first spindle **36** that projects transversely from a chassis sub-element **38**. Chassis sub-element **38** also has a second spindle **40** projecting transversely therefrom on which a second hollow axle **42** is rotatably supported. A flexible tape **44** is wound around the second hollow axle **42** which serves as a supply spool and passes to the first hollow axle **34** which serves as a take-up spool (stock bobbin). A guide plate **46** forming part of the chassis sub-element **38** helps to guide the tape **44** in a smooth passage from the supply spool to the take-up spool. The surface of the tape **44** is marked with a progression of descending numbers which denote the number of doses remaining in the aerosol canister. Typically, the starting count is 200 and successive markings on the tape decrease by one. The spacing between successive markings is coincident with the indexing motion of the matching wheel **30** so that a new number appears in a window **48** provided in the inhaler housing **2** for each successive actuation.

The ratchet-toothed wheel **30** and integrally formed first hollow axle **34** are restrained from reverse rotation by a wrap-spring clutch **50** surrounding the hollow axle **34** at the end thereof remote from ratchet-toothed wheel **30**. One end (not shown) of the wrap-spring clutch **50** is braced against the counter chassis. The windings of the wrap-spring clutch **50** are oriented such that rotation of the first hollow axle **34** in a forward sense is not resisted by the spring coils. However, reverse rotation of the hollow axle **34** acts so as to tighten the spring coils around it, thereby causing the first hollow axle **34** to be gripped by the internal surface of the wrap-spring clutch **50** and hence restraint from reverse rotation.

FIG. **3** shows a preferred embodiment of the invention set out in WO 98/28033. The dose counter **18** comprises an actuator **20** having a boss **22** integrally formed therewith and driver **28** joined to the boss **22**. The underside of boss **22** is provided with a blind hole which receives a compression spring **24** that serves to return the actuator **20** to its rest position after depression thereof during actuation of the inhaler apparatus (not shown).

The driver **28** comprises a transverse hook **52** mounted between a pair of arms **54**,**56** which are joined at their bases by a web (not shown). The web is connected to the boss **22** of the actuator **20**. A combined actuator and driver assembly may be integrally formed, such as from a plastics material, e.g. as nylon.

In use, the transverse hook **52** engages with ratchet teeth **32** of a ratchet-toothed wheel **30** which is mounted on a hollow axle **34** serving as a take-up spool for a flexible tape display **44**. At the end of the hollow axle **34** remote from the ratchet-toothed wheel **30** is a friction clutch **50** which serves to restrain the axle **34** against reverse rotation and hence prevents reverse travel of the counter tape **44**.

A control surface **58** is depicted here as a see-through element so that the workings of the dose counter may be more clearly seen. The control surface **58** extends parallel to the direction of travel of the actuator **20** and is located adjacent the ratchet-toothed wheel **30** at a position which marks a chordal projection across one of the wheel faces. One of the support arms **56** of the driver **28** is in sliding contact with control surface **58**. This sliding contact serves to inhibit the natural tendency of the driver **28** to flex radially inwardly towards the axis of rotation of the ratchet-toothed wheel **30**. By preventing such radially inward flexure, the control surface **58** restricts the engagement and disengagement of the drive **28** with the ratchet-toothed wheel **30** so that the distance by which the ratchet-toothed wheel **30** rotates is limited to one tooth pitch. This condition is observed regardless of the extent of linear travel, or stroke, of the actuator **20**.

FIG. **4** shows a schematic view of a conventional ratchet gear and drive pawl arrangement which is used in the dose counter described in WO 98/28033. The arrangement uses a reciprocating driver **28** acting in a pushing sense to rotate a ratchet-toothed wheel **30** in the direction shown by the arrows A. A fixed pawl **60** acts to prevent reverse rotation of the ratchet-toothed wheel **30** by engagement against the trailing edge **62** of a ratchet tooth **32**. However, on forward rotation of the ratchet-toothed wheel **30** in the sense of arrows A, the fixed pawl **60** is capable of radially outward deformation, urged by the leading edge **63** of a ratchet-tooth **32**.

In this arrangement, if the ratchet-toothed wheel **30** is rotated by more than a single tooth pitch but by less than two tooth pitches for each reciprocating movement of the driver **28**, there is a degree of reverse rotation until the pawl **60** becomes engaged by the trailing edge **62** (as opposed to the leading edge **63**) of a ratchet tooth **32**. Thus, the rotation of the ratchet-toothed wheel **30** may be said to be "stepped".

The components of metered-dose inhalers are manufactured to a high technical specification. However, inevitable variations in the tolerances of the components can, in some circumstances, lead to failure of the dose counter of the type disclosed in WO 98/28033. The failure of the dose counter, although not common, makes the dose counter of the type disclosed in WO 98/28033 unsuitable for some applications. There is a requirement in the art, therefore, for a dose counter with a reduced failure rate.

Accordingly, a first aspect of the present invention provides a dose counter for a metered-dose inhaler, the counter comprising:

- an actuator;
- a rotary gear;
- a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery;
- a pawl to prevent reverse rotation of the rotary gear; and
- a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear;
- wherein the pawl comprises at least two ratchet teeth which are radially spaced such that one of the teeth engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

The counter of the present invention thus provides a pawl having at least two teeth in which one and the same tooth engages with successive ratchet teeth of the wheel during the step-wise rotary motion of the wheel to prevent reverse rota-

tion of the wheel (and hence the rotary gear). By providing alternative positions for engaging the ratchet teeth of the wheel, the pawl increases the range of tolerances in the manufacture of the various components of the inhaler which can be accommodated. This in turn significantly reduces the failure rate of the dose counter and, in particular, the likelihood of undercounting. Clearly, undercounting is particularly undesirable as it can lead to a patient believing that there are more doses left within the inhaler than there actually are.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described with reference to the accompanying drawings, in which:

FIGS. **1** to **4** show a dose counter for a metered-dose inhaler according to the prior art document WO 98/28033;

FIG. **5** shows elements of a dose counter according to the present invention;

FIG. **6** shows further detail of the dose counter according to the present invention;

FIG. **7** shows a schematic representation of journeys undertaken for indexing of the dose counter to occur;

FIG. **8** shows the wheel and pawl of the dose counter of the present invention in which the pawl is (a) operating from the first tooth and (b) operating from the second tooth; and

FIG. **9** shows a metered-dose inhaler containing the dose counter of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

The dose counter of the present invention is based on that set out in FIGS. **3** and **4** described hereinabove except that the pawl **60** has been modified. Modification of the pawl followed an in-depth study of all of the components of the inhaler. Thus, as shown in FIG. **5**, the dose counter **18** of the present invention comprises an actuator **20**; a rotary gear (not shown in full in FIG. **5**); a driver **28** for driving the rotary gear in a step-wise fashion in response to displacement of the actuator **20**, the rotary gear comprising a wheel **30** mounted on a spindle (not shown), the wheel **30** having a plurality of ratchet teeth **32** around its periphery; a pawl **60** to prevent reverse rotation of the rotary gear; and a display (not shown) coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear.

The wheel **30** has a plurality of ratchet teeth **32** and preferably has 8-14 teeth (i.e. 8, 9, 10, 11, 12, 13 or 14), more preferably 9, 10, 11 or 12 teeth, and most preferably 11 teeth.

The radius of the wheel **30** measured from the centre of the wheel **30** to the tip of the teeth **32** will depend on the size of the components of the inhaler. Preferably the radius is from 1.5 to 3.5 mm, more preferably from 2.0 to 3.0 mm and most preferably 2.80±0.05 mm.

As in the dose counter 18 of WO 98/28033, the dose counter **18** of the present invention preferably further comprises a control surface to regulate the position of engagement and disengagement between the driver **28** and the wheel **30**. In addition, the driver **28** comprises a ratchet drive pawl and preferably the ratchet drive pawl is in the form of a straddle drive in which the element that engages the ratchet teeth of the wheel is supported between a pair of spaced apart support arms.

The pawl **60** comprises at least two ratchet teeth **64**,**66**. Preferably, as shown in FIG. **5**, the pawl **60** comprises two ratchet teeth **64**,**66** and no more. The at least two ratchet teeth **64**,**66** are radially spaced with respect to the ratchet-toothed wheel **30** such that one and the same tooth engages with the ratchet teeth **32** of the wheel following each step of the step-wise rotary motion of the rotary gear. Typically, one, and only one, of the ratchet teeth **64**,**66** on pawl **60** ever engages with the ratchet wheel.

FIG. **6** shows an exploded view of the dose counter **18** showing in addition to the previously described components, the stock bobbin **68** which is held taut by the action of the split hub **70**. The split hub **70** avoids the need for a clutch spring as set out in WO 98/28033. Although the clutch spring could be used as an alternative or in addition to the split hub **70**, in a preferred embodiment, the dose counter of the present invention does not include a clutch spring. The display is preferably an elongate counter tape **44** on which the dose count is printed or written, and more preferably the counter tape **44** is located on an indexing spool and the dose counter further comprises a stock bobbin to receive the counter tape as the indexing spool is advanced in a step-wise fashion.

In use, the operation of the dose counter **18** is as follows.

The user depresses the aerosol canister **6** which causes displacement of the actuator **20**. In this embodiment, the actuator **20** is adapted to engage with the rim of the medicament canister **6**. The actuator **20** is operable by linear displacement from a first position to a second position and back to the first position and movement of the rotary gear occurs either during the displacement of the actuator from the first position to the second position or during the displacement of the actuator from the second position to the first position. In the embodiment shown in FIG. **5**, the movement of the rotary gear occurs during the displacement of the actuator from the first position to the second position. In the embodiment shown, the actuator **20** comprises a spring-loaded plunger **22**,**24**, the plunger being depressible against the return force of the spring loading when the actuator is caused to deliver a dose of medicament.

During the movement from the first position to the second position, the actuator **20** causes the driver **28** to engage the trailing edge **62** of the ratchet tooth **32** of the wheel **30**. As the actuator **20** and driver **28** move down the ratchet-toothed wheel **30** rotates.

The spindle of the rotary gear moves the counter tape **44** revealing the next integer. The counter tape **44** is held taut by the action of the split hub **70** on which is mounted the stock bobbin **68**.

The pawl **60** radially outwardly deforms to allow the wheel **30** to rotate by one tooth **32**. The at least two teeth **64**,**66** of pawl **60** may be inherently resilient to allow the required radially outward deformation and return. Alternatively or in addition, the pawl **60** may be mounted on a resilient support capable of radially outward deformation, for example the resilient support may be a resilient flange incorporated in to the chassis of the dose counter **18**.

The driver **28** releases the ratchet-toothed wheel **30** after it has engaged with the pawl **60**. On reset of the inhaler, the canister **6** is allowed to return to its initial (first) position. The compression spring **24** pushes the actuator **20** to follow the canister. The driver **28** on the actuator **20** flexes to pass over the teeth of the ratchet-toothed wheel **30** as the actuator **20** moves from the first to the second position.

The tooth of the at least two teeth **64**,**66** which has engaged tooth **32** of the wheel **30** prevents the rotary gear from rotating backwards.

The counter mechanism of the type described with reference to WO 98/28033 and in accordance with the present invention must rotate the wheel **30** of the rotary gear by exactly one tooth spacing each time the actuator is depressed. By tooth spacing is meant one tooth pitch, i.e. the radial

distance between the same notional point two adjacent teeth **32** on the ratchet-toothed wheel **30**. The stroke available for indexing the rotary gear is equal to the full stroke of the actuator **2**. Where the metered-dose inhaler is a pressurised inhaler, the stroke available for counting is equal to the full stroke of the medicament canister **6**. However, there are three movements (or "journeys") that must be completed within this total distance for indexing of the dose counter to occur. The three journeys are shown schematically in FIG. **7**.

FIG. **7** shows a graphical representation the amount of canister travel and the excess stroke available before the three critical journeys must occur. Firstly, the canister travel must close the start gap which is the sum of the tolerances of the manufactured components in the vertical direction. Secondly, the stroke must take up any lost motion, such as in pivot play, flexing of the pawl and arc motion of the drive pawl. Thirdly, is the so-called "stroke to count", which is the journey which leads to indexing of the rotary gear by one tooth spacing.

The stroke available for counting will clearly depend on the type of metered-dose inhaler used. By way of example, a suitable inhaler is the pressurised metered-dosed inhaler EasiBreathe® which uses a Qvar® canister. The canister stroke in this inhaler was measured as 3.04±0.255 mm. This tolerance represents ±3 standard deviations so that 99.7% of all canister strokes will lie within these limits. The measurements were taken from force versus displacement profiles for Qvar® canisters. One hundred and fifty canisters were measured at the start, middle and end of life giving a total of 450 stroke measurements.

The start gap is the tolerance stack in the vertical direction and includes a first distance between the part of the driver **28** which engages the wheel **30** and the appropriate ratchet tooth **32** of the wheel **30** of the rotary gear, and a second distance between the top of the actuator **20** and the canister **6**. The tolerance in the vertical direction was found to be ±0.47 mm. The nominal start gap for the EasiBreathe® inhaler is set at 0.85 mm and hence the start gap with tolerances is 0.85±0.47 mm.

Thus, since the start gap is 0.85±0.47 mm the maximum start gap (mean plus 3 standard deviations) is 1.32 mm (0.85±0.47). When such a start gap occurs, a short-stroking canister (for example, 2.79 mm) will not rotate the wheel **30** of the rotary gear by a full tooth spacing. This will lead to failure of the dose counter. However, the provision of a first and second ratchet tooth **64**,**66** in the pawl **60** allows the ratchet tooth **32** of the wheel **30** of the rotary gear to rest on the second tooth **66**. In the present embodiment, the second tooth **66** is 0.60 mm away from the first tooth **64**. Thus, for the next actuation, the start gap is reduced to 0.72 mm (1.32−0.60). The stroke is therefore sufficient to rotate the wheel **30** a full index starting from this point. The step-wise rotation of the wheel **30** then continues with all subsequent actuations starting and finishing with the ratchet teeth **32** of the wheel **30** of the rotary gear engaged with the second tooth **66** of the pawl **60**.

FIG. **8** shows a more detailed view of the wheel **30** of the rotary gear, the driver **28** and the pawl **60** to prevent reverse rotation of the rotary gear. In FIG. **8**(*a*) the ratchet tooth **32***a* of the wheel **30** is engaged with the first ratchet tooth **64** of the pawl. In FIG. **8**(*b*) the same tooth **32***a* of the wheel **30** is engaged with the second ratchet tooth **66** of the pawl **60**. It may be seen that the start gap is reduced in the arrangement shown in FIG. **8**(*b*) in comparison with the same distance in FIG. **8**(*a*). The second tooth **66** of the pawl **60** therefore allows the first distance S of the start gap (the between the part of the driver **28** which engages the wheel **30** and the appropriate ratchet tooth **32** of the wheel **30**) to be reduced thereby accommodating a greater tolerance in the canister stroke.

As explained hereinabove, the first and second teeth **64**,**66** provide different starting positions for the wheel **30** of the rotary gear to accommodate different tolerance levels in the components of the inhaler. The teeth **64**,**66** are therefore separated radially with respect to the wheel **30**. The spacing will clearly depend on the precise nature of the components used in the inhaler and hence it would be inappropriate to provide a precise numerical value. It is clear from the mechanism, however, that the radial spacing will be less than the radial distance between adjacent teeth **32** on the wheel **30** of the rotary gear.

In the embodiments shown herein, the dose counter **18** of the present invention incorporates a pawl **60** having two teeth **64**,**66** and only two teeth, i.e. the pawl **60** consists essentially of two teeth **64**,**66**. However, additional teeth could be incorporated to provide additional precision to the start position of the wheel **30** and thus additional precision in the first distance S. For example, the pawl may have 2-6, preferably two, three or four teeth, more preferably two or three and most preferably two teeth.

In a particularly preferred embodiment of the present invention, the dose counter is adapted for a canister stroke of 3.041±0.256 mm: the wheel of the rotary gear has a radius of 2.80±0.05 mm defined as the distance from the centre of the wheel to the tip of the teeth and 11 ratchet teeth around its periphery; and the pawl comprises two ratchet teeth only which have a radial spacing of 0.6 mm. In this embodiment, the total stroke to guarantee a count is 2.372±0.115 mm. The probability of failure to count or resent due to component dimension variations (manufacturing tolerances) is less than 1 in 10 million.

The present invention further provides a metered dose inhaler **72** as shown in FIG. **9**. The inhaler comprises a medicament canister **6**, an actuator body **74** for receiving the canister **6** and having a medicament delivery outlet, and the dose counter as described herein. The inhaler has a window **76** for viewing the integers on the tape **44**. In a preferred embodiment the actuator body **74** comprises a sump and preferably a smooth rounded sump. Typically, a rounded sump is understood to have a substantially cylindrical upper portion and a substantially hemi-spherical lower portion. Typically, smooth is understood to mean that the surface is sufficiently free of surface protrusions to the extent that during normal use medicament will not substantially adhere thereto.

In one embodiment of the invention the vessel contains a medicament in the form of an aerosol. Alternatively in another embodiment of the invention the vessel contains a medicament in the form of a dry powder.

The medicament may be any medicament that is suitable to be delivered to a patient via a metered-dose inhaler. In particular medicaments for the treatment of a wide variety of respiratory disorders are delivered in this manner including anti-allergic agents (e.g. cromoglycate, ketotifen and nedocromil), anti-inflammatory steroids (e.g. beclomethasone dipropionate, fluticasone, budesonide, flunisolide, ciclesonide, triamcinolone acetonide and mometasone furoate); bronchodilators such as: β_2-agonists (e.g. fenoterol, formoterol, pirbuterol, reproterol, salbutamol, salmeterol and terbutaline), non-selective β-stimulants (e.g. isoprenaline), and xanthine bronchodilators (e.g. theophylline, aminophylline and choline theophyllinate); and anticholinergic agents (e.g. ipratropium bromide, oxitropium bromide and tiotropium).

A further aspect of the present invention provides the use of a pawl **60** comprising at least two ratchet teeth **64**,**66** for preventing miscounting in a dose counter of a metered dose inhaler **72**. A still further aspect of the present invention provides the use of a pawl **60** comprising at least two ratchet teeth **64**,**66** for preventing undercounting in a counter of a metered dose inhaler **72**.

In a preferred embodiment the counter comprises an actuator **20**; a rotary gear; a driver **28** for driving the rotary gear in a step-wise fashion in response to displacement of the actuator **20**, the rotary gear comprising a wheel **30** mounted on a spindle **36** which wheel **30** having a plurality of ratchet teeth **32** around its periphery; and a display **44** coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear. Preferably, the pawl **60** prevents reverse rotation of the rotary gear.

Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention as defined by the appended claims.

The invention claimed is:

1. A dose counter for a metered-dose inhaler, the counter comprising: an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery; a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear; wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

2. A dose counter as claimed in claim **1**, wherein the pawl comprises two ratchet teeth and no more.

3. A dose counter as claimed in claim **1**, wherein the pawl is mounted on a resilient support.

4. A dose counter as claimed in claim **3**, wherein the resilient support is a resilient flange incorporated into the body of the dose counter.

5. A dose counter as claimed in claim **1**, further comprising a control surface to regulate the position of engagement and disengagement between the driver and the wheel.

6. A dose counter as claimed in claim **1**, wherein the actuator is operable by linear displacement from a first position to a second position and back to the first position and wherein movement of the rotary gear occurs either during the displacement of the actuator from the first position to the second position or during the displacement of the actuator from the second position to the first position.

7. A dose counter as claimed in claim **1**, wherein the actuator comprises a spring-loaded plunger, the plunger being depressible against a return force of a spring of the spring-loaded plunger when the actuator is caused to deliver a dose of medicament.

8. A dose counter as claimed in claim **1**, wherein the driver comprises a ratchet drive pawl.

9. A dose counter as claimed in claim **8**, wherein the ratchet drive pawl is in the form of a straddle drive in which an element that engages the ratchet teeth of the wheel is supported between a pair of spaced apart support arms.

10. A dose counter as claimed in claim **1**, wherein the display is an elongate counter tape on which a dose count is printed or written.

11. A dose counter as claimed in claim **10**, wherein the counter tape is located on an indexing spool and the dose counter further comprises a stock bobbin to receive the counter tape as the indexing spool is advanced in a step-wise fashion.

12. A dose counter as claimed in claim **1**, wherein the actuator is adapted to engage with a rim of a medicament canister.

13. A dose counter as claimed in claim **1**, wherein the wheel of the rotary gear has eight to fourteen ratchet teeth around a periphery of the rotary gear.

14. A dose counter as claimed in claim **13**, wherein the wheel of the rotary gear has eleven ratchet teeth around its periphery.

15. A dose counter as claimed in claim **1**, wherein the wheel of the rotary gear has a radius defined as the distance from the centre of the wheel to a tip of the teeth of 2.80+−0.05 mm and eleven ratchet teeth around its periphery, and the pawl comprises two ratchet teeth and no more which have a radial spacing of about 0.6 mm.

16. A metered dose inhaler comprising a medicament canister, an actuator body for receiving the canister and having a medicament delivery outlet, and the dose counter as claimed in claim **1**.

17. A metered dose inhaler according to claim **16** wherein the actuator body comprises a smooth rounded sump.

18. The use of a dose counter for preventing miscounting in a metered dose inhaler, the dose counter comprising: an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery; a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear; wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

19. The use of a dose counter for preventing undercounting in a metered dose inhaler, the dose counter comprising: an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery; a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear; wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

* * * * *

Exhibit B

US009463289B2

(12) **United States Patent**
Walsh et al.

(10) **Patent No.: US 9,463,289 B2**
(45) **Date of Patent: Oct. 11, 2016**

(54) **DOSE COUNTERS FOR INHALERS, INHALERS AND METHODS OF ASSEMBLY THEREOF**

(71) Applicants: **IVAX PHARMACEUTICALS IRELAND**, Utrecht (NL); **NORTON WATERFORD**, Utrecht (NL); **TEVA PHARMACEUTICALS IRELAND**, Utrecht (NL)

(72) Inventors: **Declan Walsh**, County Kilkenny (IE); **Derek Fenlon**, County Wexford (IE); **Simon Kaar**, County Cork (IE); **Jan Geert Hazenberg**, County Kilkenny (IE); **Daniel Buck**, County Waterford (IE); **Paul Clancy**, Waterford (IE); **Robert Charles Uschold**, Leominster, MA (US); **Jeffrey A. Karg**, Hopkinton, MA (US)

(73) Assignees: **IVAX Pharmaceuticals Ireland**, Waterford (IE); **Norton (Waterford) Limited**, Waterford (IE); **Teva Pharmaceuticals Ireland**, Waterford (IE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/103,324**

(22) Filed: **Dec. 11, 2013**

(65) **Prior Publication Data**

US 2014/0096769 A1 Apr. 10, 2014

Related U.S. Application Data

(62) Division of application No. 13/110,532, filed on May 18, 2011, now Pat. No. 8,978,966.

(60) Provisional application No. 61/345,763, filed on May 18, 2010, provisional application No. 61/417,659, filed on Nov. 29, 2010.

(51) **Int. Cl.**
G06M 1/06 (2006.01)
A61M 11/00 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61M 15/0071*** (2014.02); ***A61M 11/00*** (2013.01); ***A61M 15/009*** (2013.01);
(Continued)

(58) **Field of Classification Search**
USPC 235/8, 103; 128/200.23
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,174,890 A 11/1979 Johnson
4,669,838 A 6/1987 Hibbard
(Continued)

FOREIGN PATENT DOCUMENTS

CA 2501726 9/2006
EP 1330280 11/2004
(Continued)

OTHER PUBLICATIONS

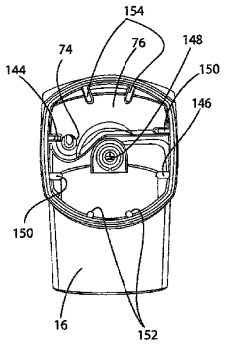
First Examination Report of counterpart New Zealand Patent Application No. 603466, dated Jul. 1, 2013.
(Continued)

Primary Examiner — Daniel Hess
(74) *Attorney, Agent, or Firm* — RatnerPrestia

(57) **ABSTRACT**

A manually operated metered dose inhaler includes a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and including a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

10 Claims, 17 Drawing Sheets



(51) **Int. Cl.**
A61M 15/00 (2006.01)
G06M 1/24 (2006.01)

(52) **U.S. Cl.**
CPC ***A61M15/0025*** (2014.02); ***A61M 15/0026*** (2014.02); ***A61M 15/0065*** (2013.01); ***A61M 15/0078*** (2014.02); ***G06M 1/246*** (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,687,359	A	8/1987	Barrus	
5,482,030	A	1/1996	Klein	
5,861,911	A	1/1999	Oosaka	
6,446,627	B1	9/2002	Bowman et al.	
6,718,972	B2	4/2004	O'Leary	
8,418,690	B2	4/2013	Power	
8,474,448	B2	7/2013	Oi	
2002/0047021	A1	4/2002	Blacker et al.	
2002/0078949	A1	6/2002	OLeary	
2002/0078950	A1	6/2002	OLeary	
2003/0209239	A1	11/2003	Rand	
2004/0095746	A1	5/2004	Murphy	
2005/0028815	A1	2/2005	Deaton et al.	
2005/0087191	A1	4/2005	Morton et al.	
2006/0096594	A1	5/2006	Bonney et al.	
2006/0107949	A1*	5/2006	Davies et al.	128/200.23
2006/0107979	A1	5/2006	Kim	
2007/0062518	A1	3/2007	Geser	
2008/0242465	A1	10/2008	Strobel	
2009/0178678	A1	7/2009	O'Leary	
2010/0089395	A1	4/2010	Power	
2010/0218759	A1	9/2010	Anderson et al.	
2011/0041845	A1	2/2011	Solomon	
2012/0006322	A1	1/2012	Anderson	

FOREIGN PATENT DOCUMENTS

EP	1486227	12/2004
GB	2320489 A	6/1998
JP	02502129	7/1990
JP	450059	8/1992
JP	07100205	4/1995
JP	10504220	4/1998
JP	2002528144	9/2002
JP	2004501685	1/2004
JP	2008094103	4/2008
JP	2008261423	10/2008
JP	2009233308	10/2009
JP	2009257392	11/2009
JP	2010096308	4/2010
WO	8909078	10/1989
WO	9628205	9/1996
WO	WO 9828033	7/1998
WO	9936115	7/1999
WO	03101514	12/2003
WO	2005102430	11/2005
WO	WO 2006/062449	6/2006
WO	2007012861	2/2007
WO	2007062518	6/2007
WO	WO 2008/023019	2/2008
WO	WO 2008119552	10/2008
WO	2011012325	2/2011
WO	2011012327	2/2011

OTHER PUBLICATIONS

Entire patent prosecution history of U.S. Appl. No. 14/699,567, filed Apr. 29, 2015, entitled, "Dose Counter for Inhaler and Method for Counting Doses."
Entire patent prosecution history of U.S. Appl. No. 14/699,578, filed, Apr. 29, 2015, entitled, "Dose Counter for Inhaler Having a Bore and Shaft Arrangement."
Entire patent prosecution history of U.S. Appl. No., 14/699,584, filed Apr. 29, 2015, entitled, "Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator."
Entire patent prosecution history of U.S. Appl. No. 14/713,612, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/713,620, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/713,633, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/713,643, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 13/110,532, filed May 18, 2011, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,343, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,353, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,363, filed Dec. 1, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,392, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
European Patent Office Communication, dated Apr. 24, 2014 of counterpart European Patent Application No. 11 010 211.8.
European Patent Office Communication, dated Apr. 24, 2014 of counterpart European Patent Application No. 11 010 212.6.

* cited by examiner

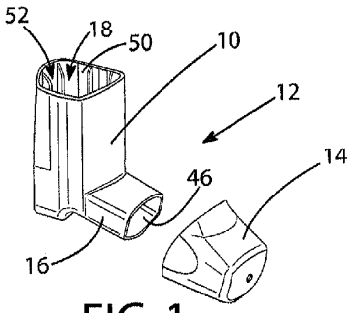


FIG. 1

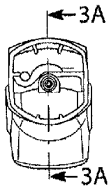


FIG. 2

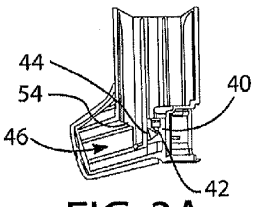


FIG. 3A

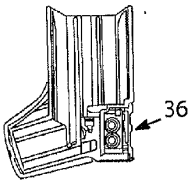


FIG. 3B

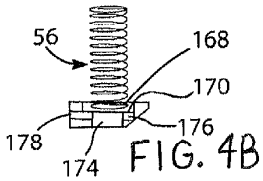


FIG. 4B

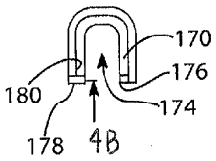


FIG. 4C

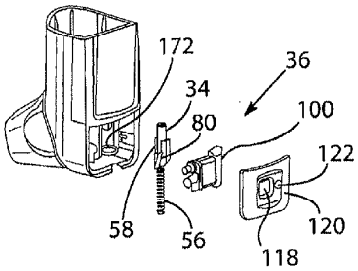


FIG. 4A

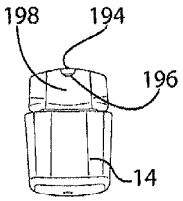


FIG. 5

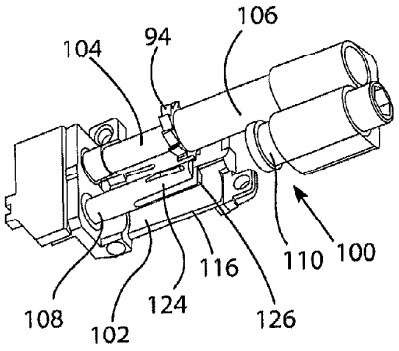


FIG. 6A

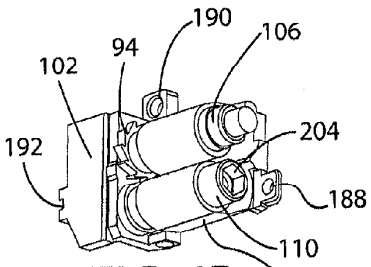


FIG. 6B

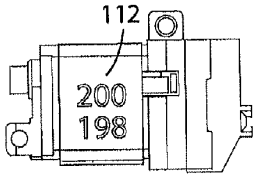


FIG. 6C

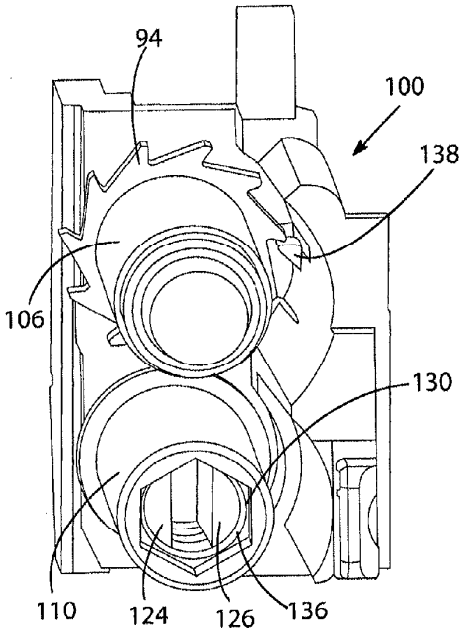


FIG. 6D

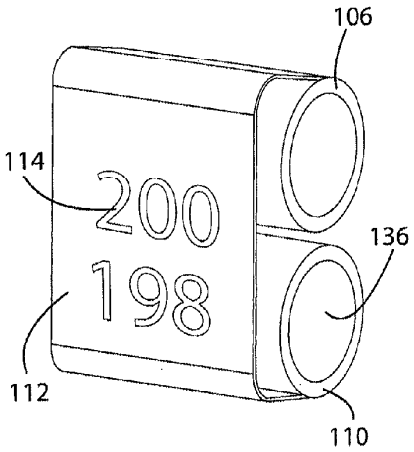


FIG. 6E

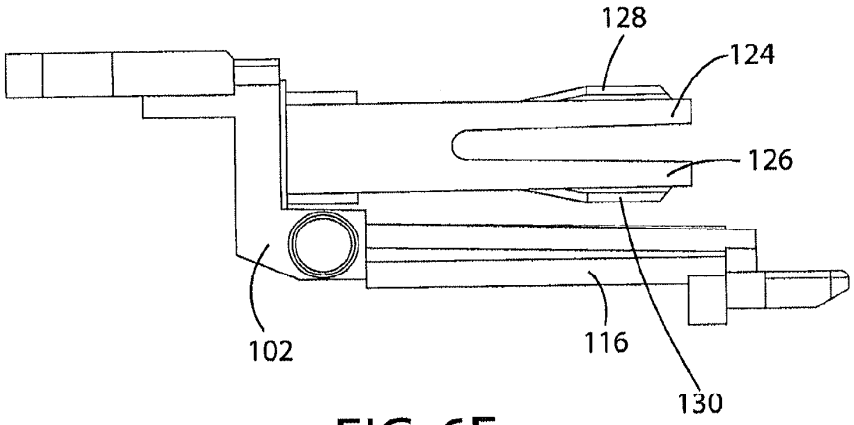


FIG. 6F

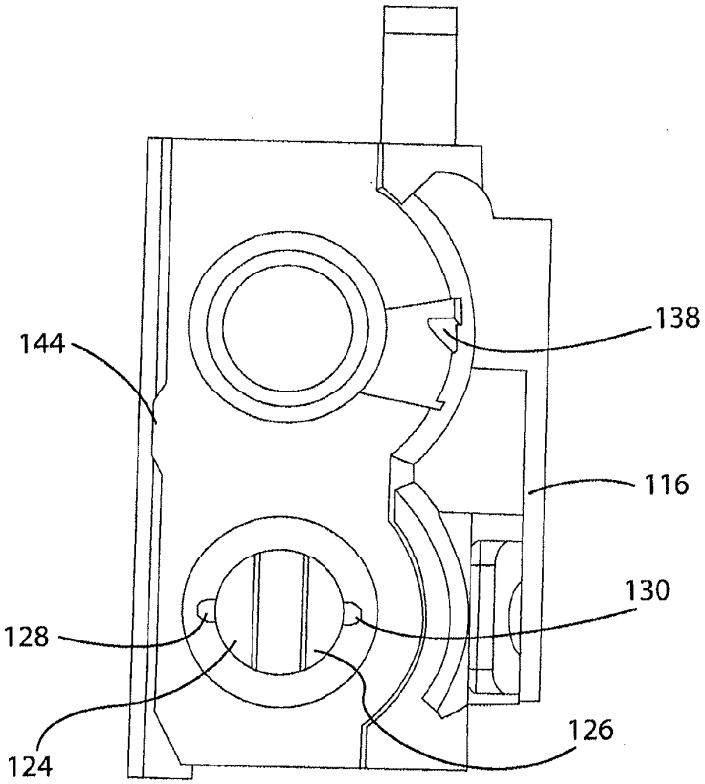


FIG. 6G

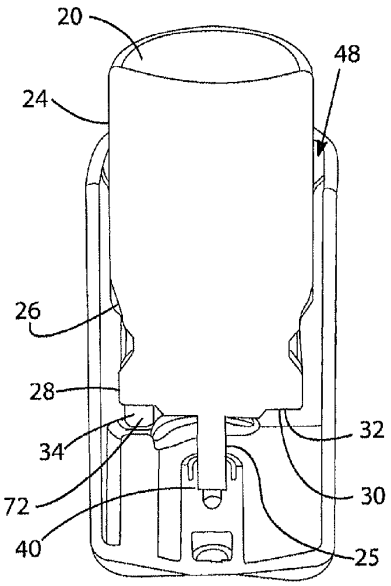


FIG. 7A

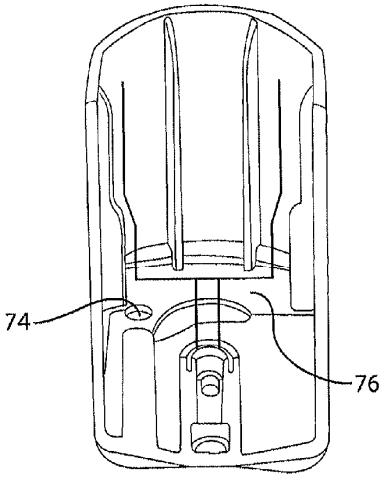


FIG. 7B

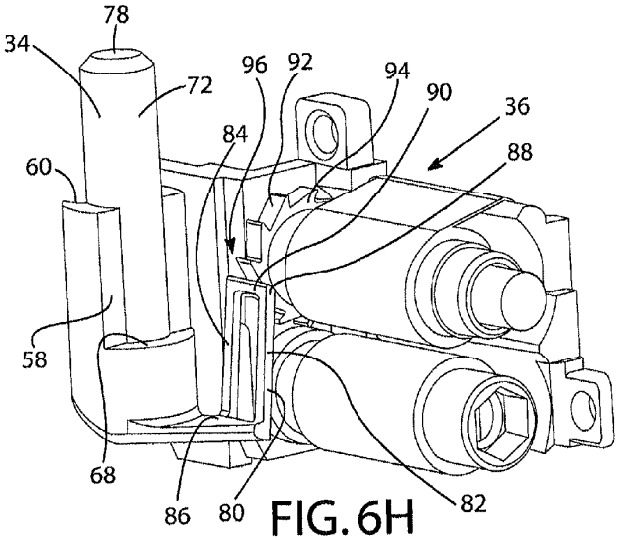


FIG. 6H

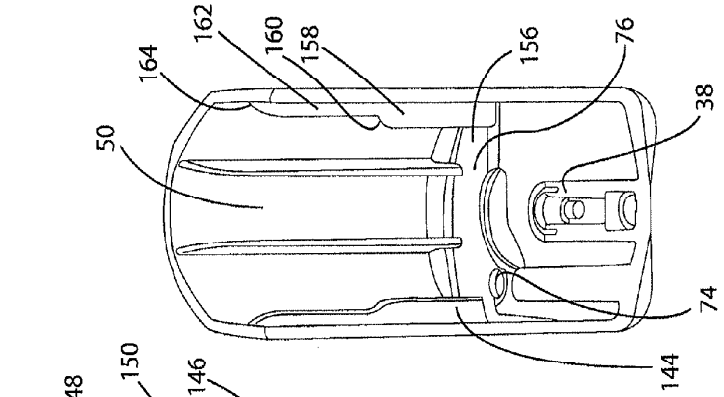


FIG. 7C

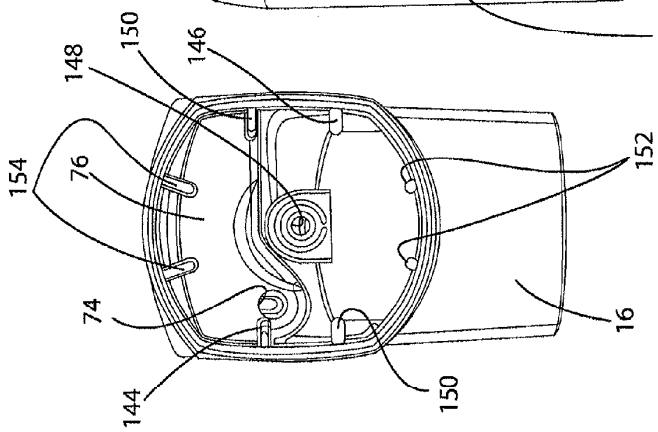


FIG. 7D

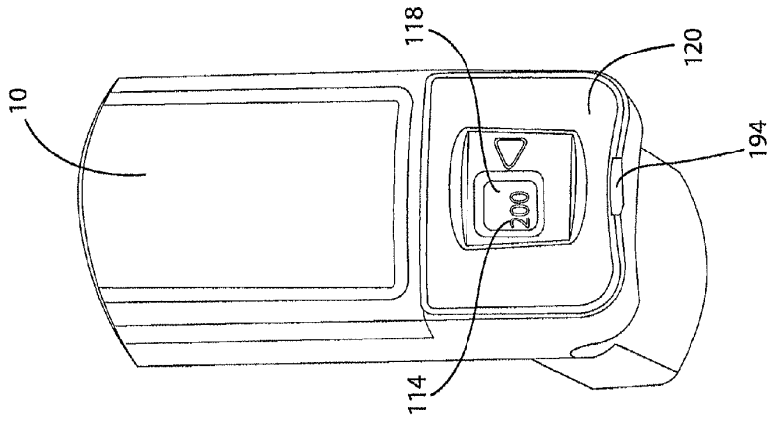


FIG. 8D

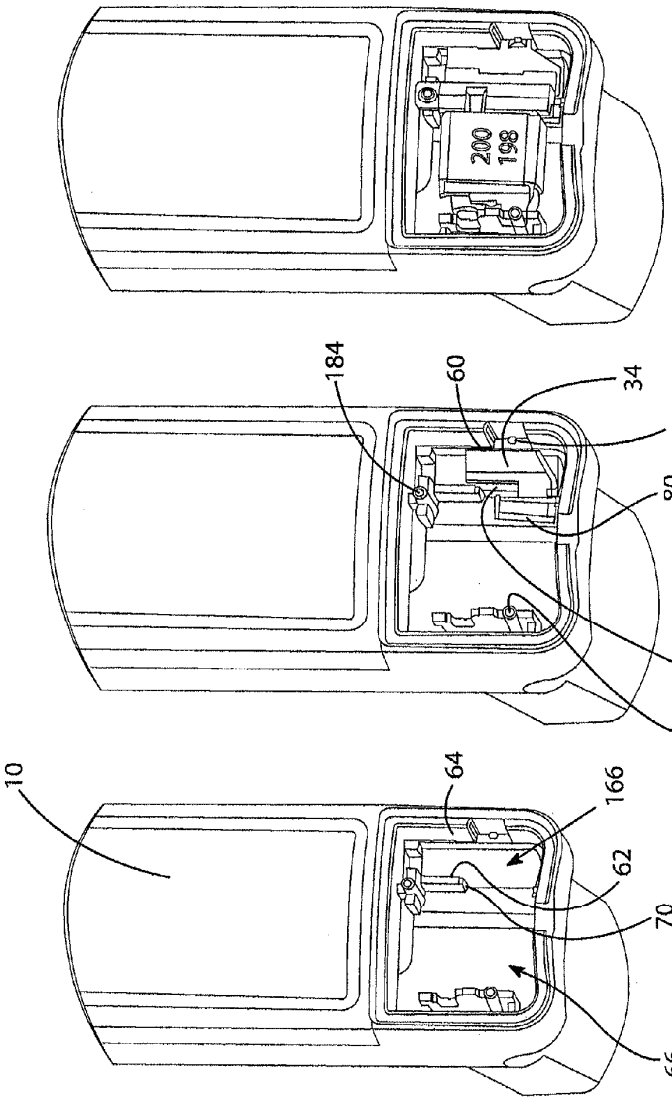


FIG. 8C

FIG. 8B

FIG. 8A

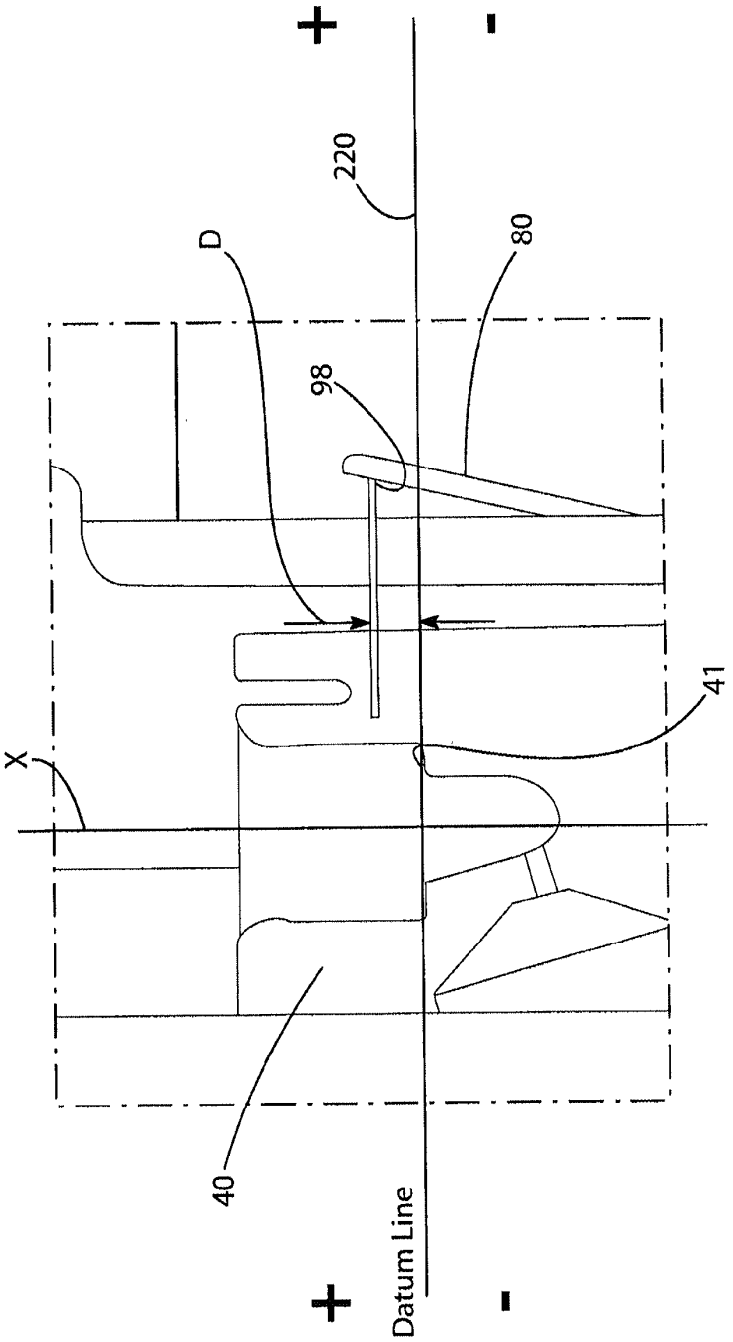


FIG. 9

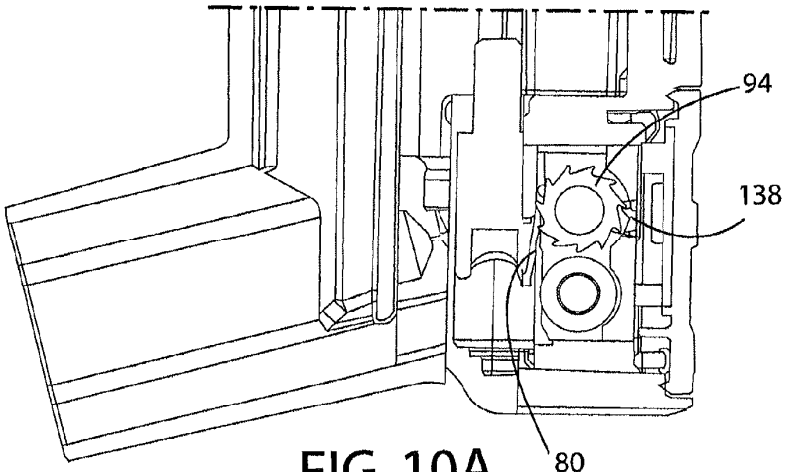


FIG. 10A

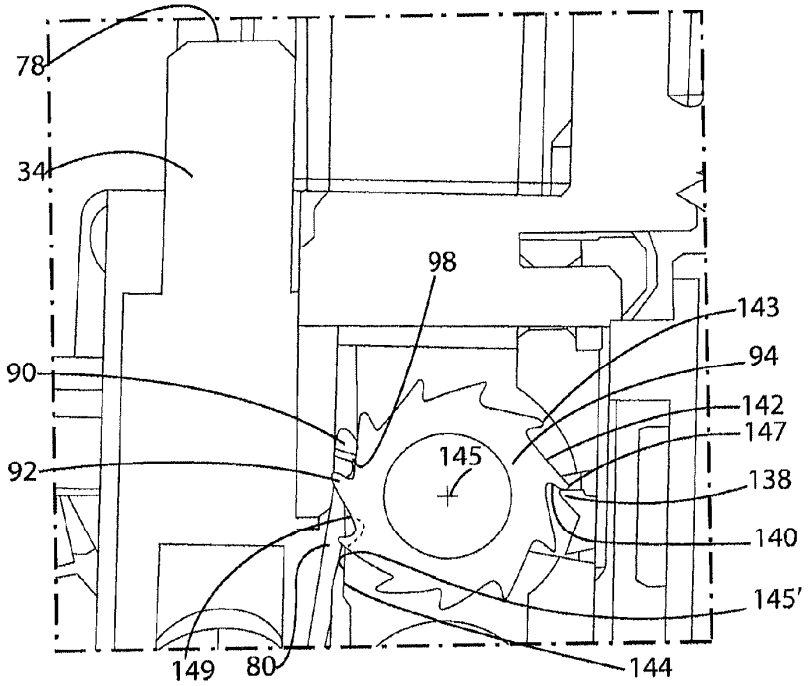


FIG. 10B

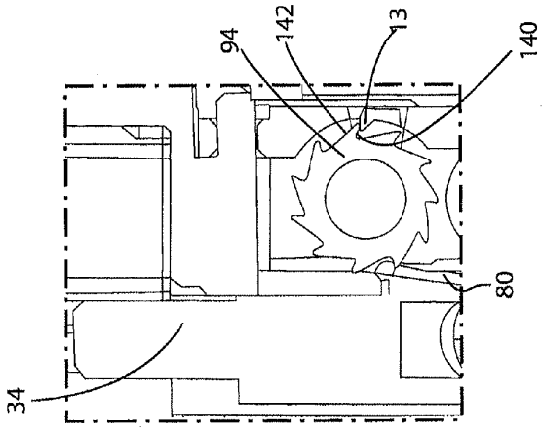


FIG. 10E

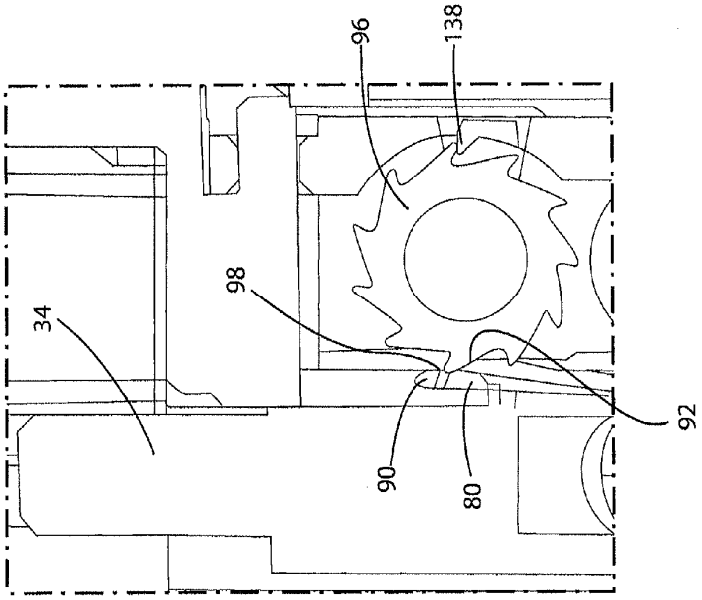


FIG. 10C

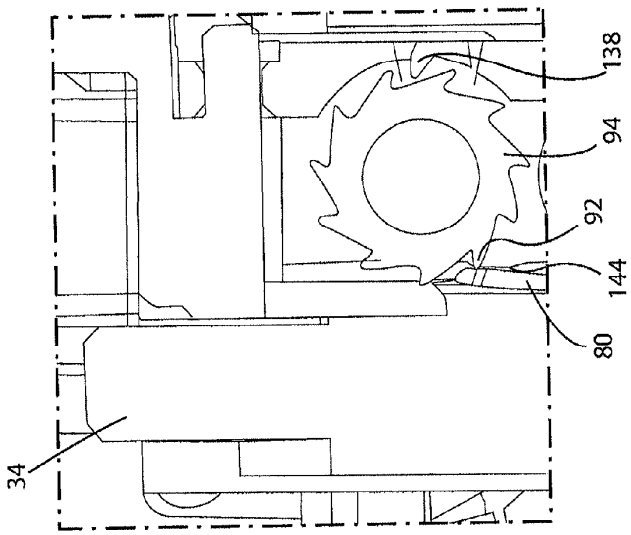


FIG. 10F

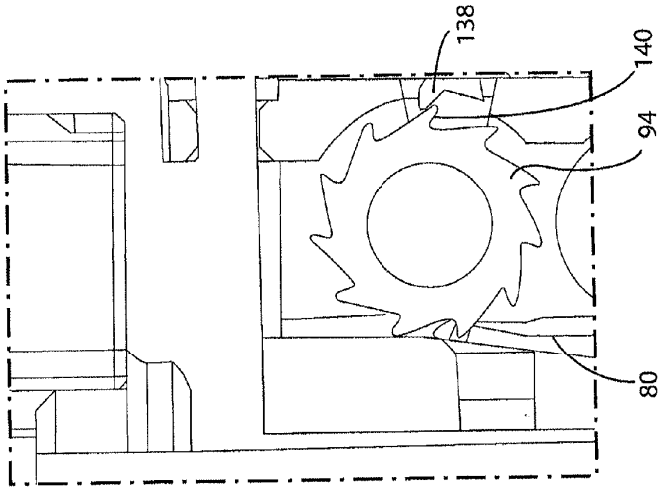


FIG. 10D

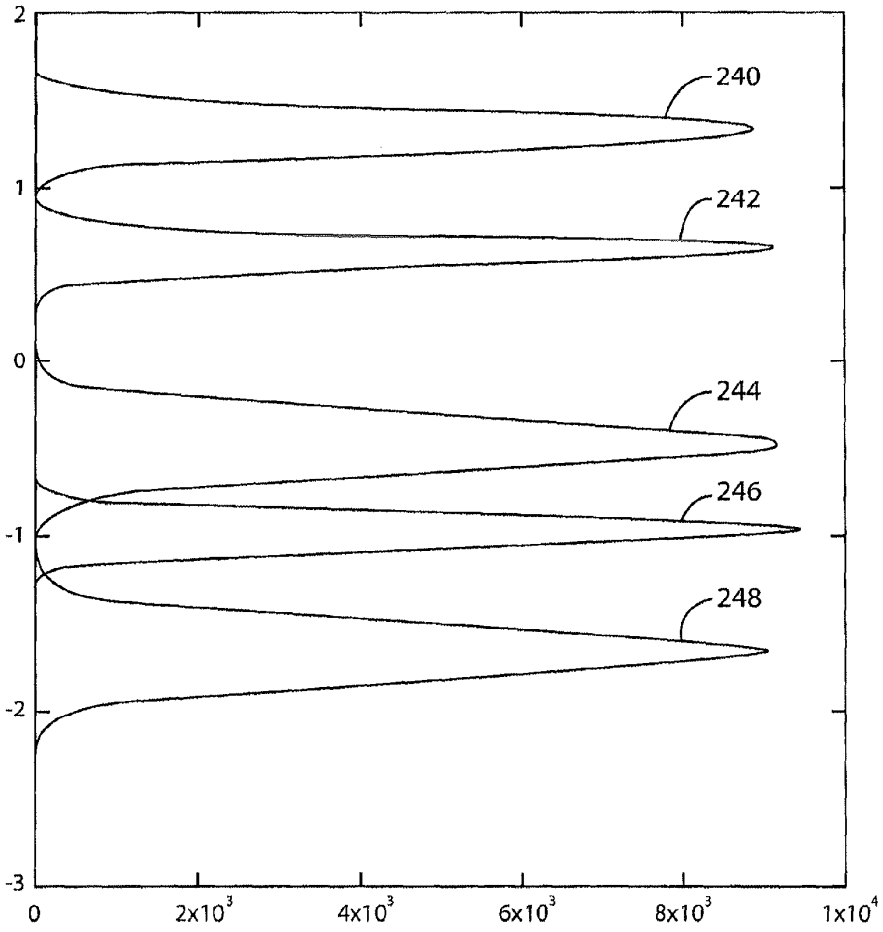

2
1
0
-1
-2
-3
0
2x10^3
4x10^3
6x10^3
8x10^3
1x10^4
240
242
244
246
248

FIG. 11

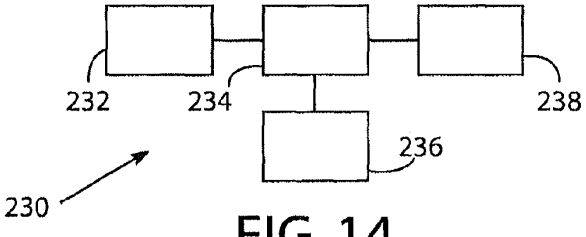

232
234
238
236
230

FIG. 14

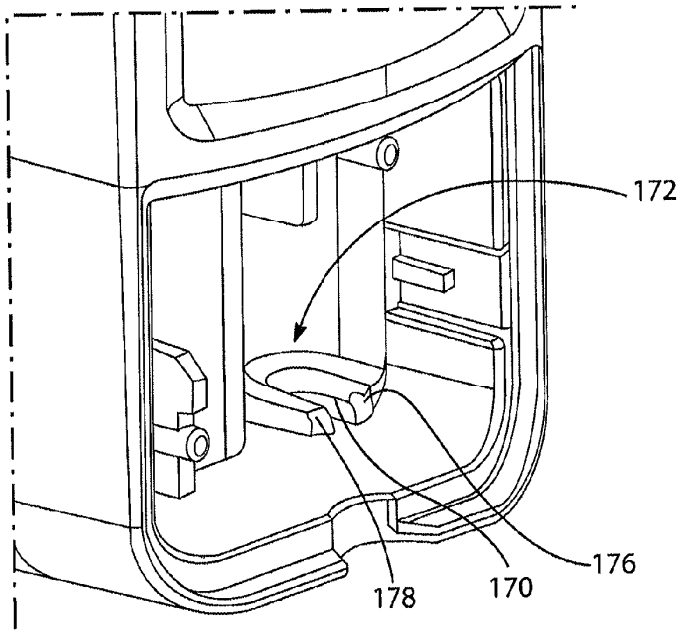


FIG. 12

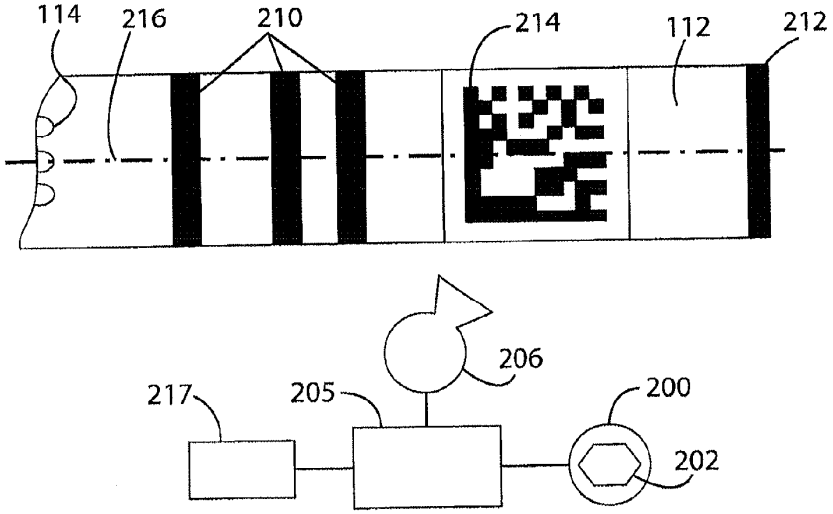


FIG. 13

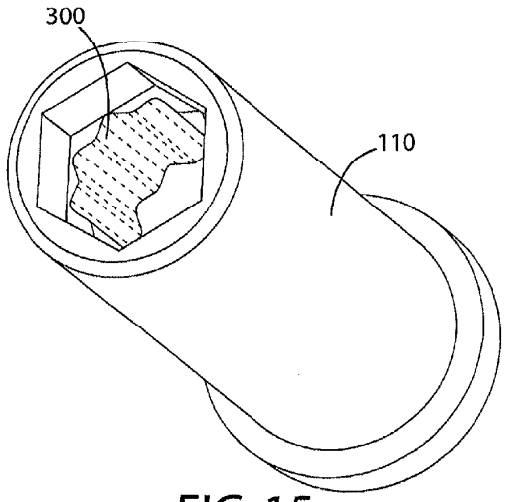


FIG. 15

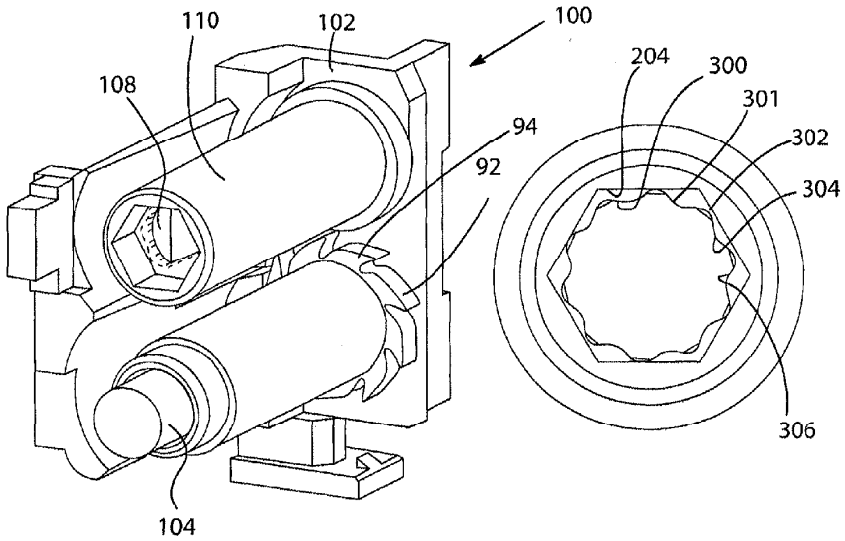


FIG. 20

FIG. 16

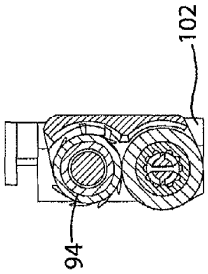


FIG. 19A

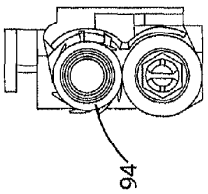


FIG. 19B

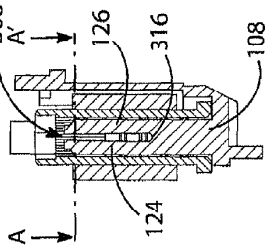


FIG. 19C

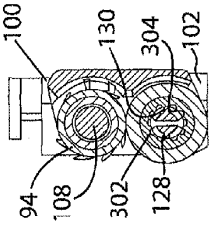


FIG. 18A

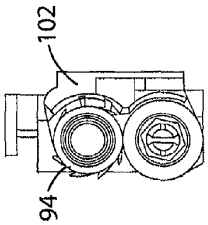


FIG. 18B

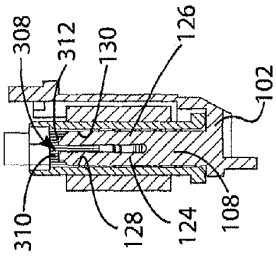


FIG. 18C

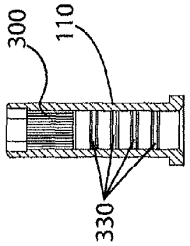


FIG. 17

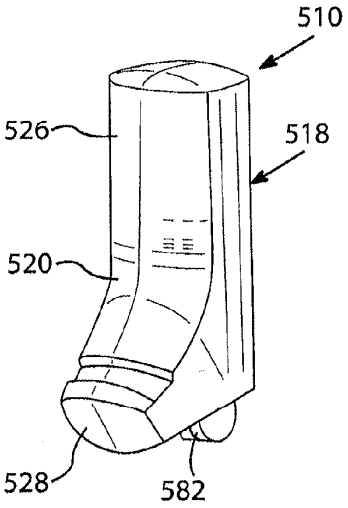

510
526
518
520
528
582

FIG. 21

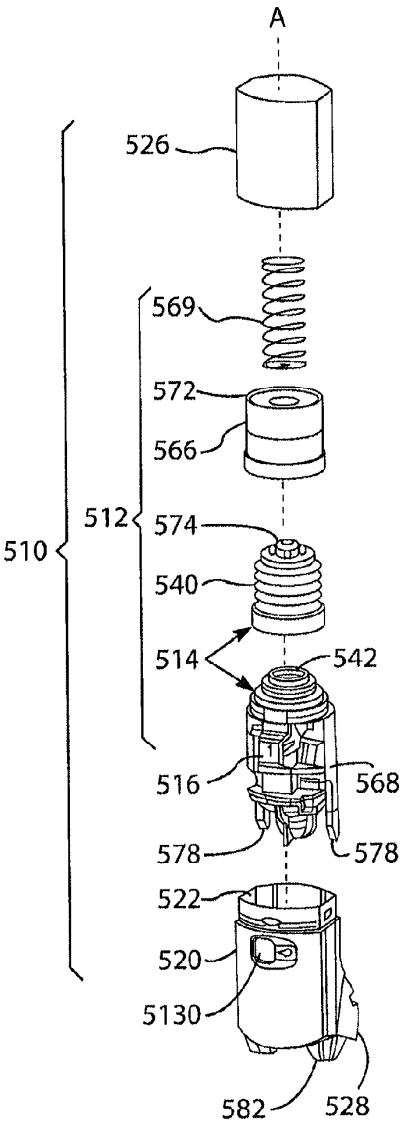

A
526
569
572
566
512
574
510
540
514
542
516
568
578
578
522
520
5130
582
528

FIG. 22

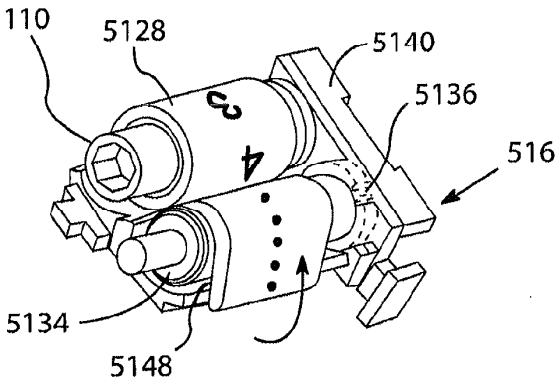

110
5128
5140
5136
516
5134
5148

FIG. 23

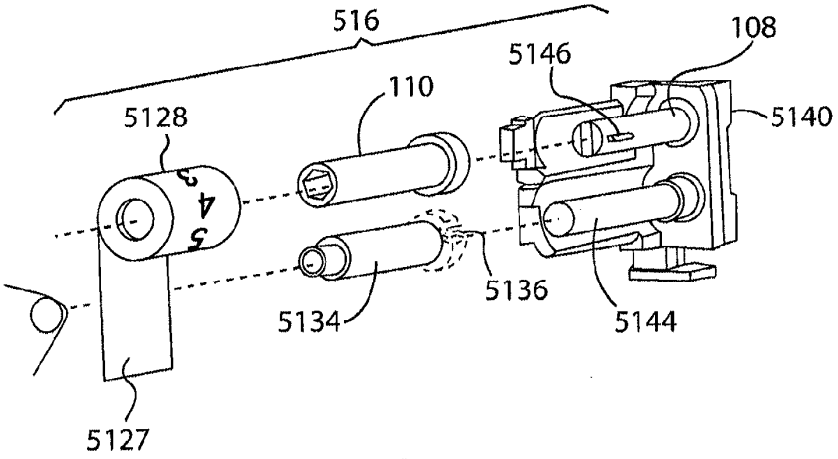

516
108
5146
110
5128
5140
5136
5134
5144
5127

FIG. 24

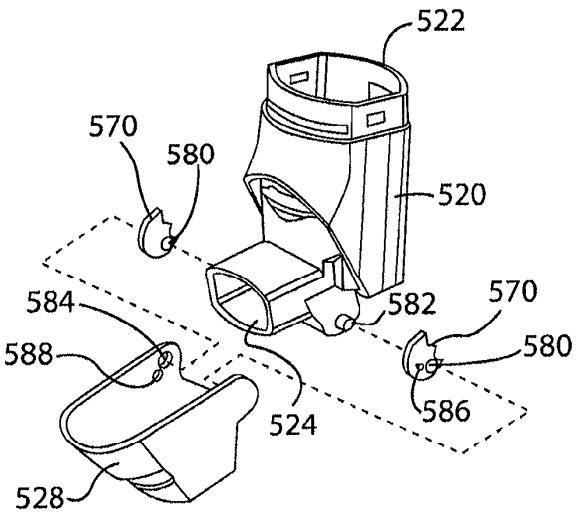


FIG. 25

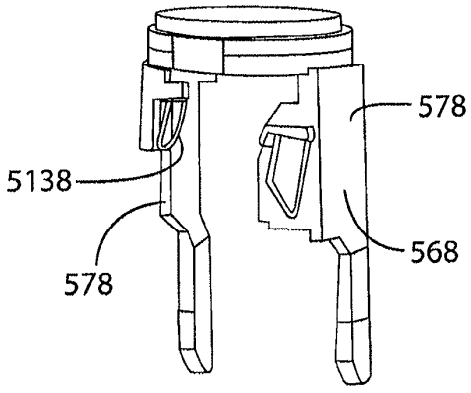


FIG. 26

DOSE COUNTERS FOR INHALERS, INHALERS AND METHODS OF ASSEMBLY THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a divisional patent application of U.S. Non-Provisional patent application Ser. No. 13/110,532, filed May 18, 2011, which claims priority to U.S. Provisional Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Provisional Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-dawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/280733 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler is closed. Due to the way in which the mouthpiece is opened and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/−0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections maybe provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or concavities regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter

which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an otherwise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf my also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is be highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is high advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia arc in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia. The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. **1** is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. **2** is a top plan view of the components as shown in FIG. **1**;

FIG. **3**A is a section on the plane **3**A-**3**A in FIG. **2**;

FIG. **3**B is a view corresponding to FIG. **3**A but with a dose counter fitted to the main body of the inhaler;

FIG. **4**A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. **4**B is a view in the direction **4**B in FIG. **4**C of a spring retainer of the dose counter;

FIG. **4**C is a top view of the spring retainer of FIG. **4**B;

FIG. **5** is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. **6**A, **6**B, **6**C, **6**D, **6**E, **6**F, **6**G and **6**H are various views of dose counter components of the inhaler;

FIGS. **7**A and **7**B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. **7**C is a further sectional view similar to that of FIG. **7**B but with the canister removed;

FIG. **7**D is a top plan view of the inhaler main body;

FIGS. **8**A, **8**B, **8**C and **8**D show the inhaler main body and dose counter components during assembly thereof;

FIG. **9** shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. **10**A, **10**B, **10**C, **10**D, **10**E and **10**F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. **11** shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. **12** is an enlarged version of part of FIG. **4**A;

FIG. **13** shows an end portion of a tape of the dose counter;

FIG. **14** shows a computer system for designing the dose counter;

FIG. **15** is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. **1** to **14**;

FIG. **16** shows an end view of the stock bobbin of FIG. **15**;

FIG. **17** is a section through a longitudinal axis of the stock bobbin of FIGS. **15** and **16**;

FIGS. **18**A to **18**C are views of the stock bobbin of FIGS. **15** to **17** mounted in the dose counter chassis of FIGS. **1** to **14**, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. **6**F, with the forks in a compressed configuration;

FIGS. **19**A to **19**C are views equivalent to FIGS. **18**A to **18**C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. **20** is an isometric view of the chassis assembled and including the stock bobbin of FIGS. **15** to **17** but excluding the tape for reasons of clarity;

FIG. **21** is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. **22** is an exploded view of the inhaler of FIG. **21**;

FIG. **23** is a view of a dose counter of the inhaler of FIG. **21**;

FIG. **24** is an exploded view of the dose counter shown in FIG. **23**;

FIG. **25** is an exploded view of parts of the inhaler of FIG. **21**; and

FIG. **26** is a view of a yoke of the inhaler of FIG. **21**.

DETAILED DESCRIPTION OF THE INVENTION

FIG. **1** shows a main body **10** of a manually operated metered dose inhaler **12** in accordance with an embodiment related to the present invention and having a mouthpiece cap **14** securable over a mouthpiece **16** of the main body.

The main body has a canister chamber **18** into which a canister **20** (FIG. **7**A) is slideable. The canister **20** has a generally cylindrical main side wall **24**, joined by a tapered section **26** to a head portion **28** having a substantially flat lower face **30** which has an outer annular drive surface **32** arranged to engage upon and drive an actuation pin **34** of a dose counter **36** as will be described. Extending centrally and axially from the lower face **30** is a valve stem **38** which is arranged to sealingly engage in a valve stem block **40** of the main body **10** of the inhaler **12**. The valve stem block **40** has a passageway **42** leading to a nozzle **44** for directing the contents of the canister **20**, namely active drug and propellant, towards an air outlet **46** of the inhaler main body **12**. It will be appreciated that due to gaps **48** between the canister **20** and an inner wall **50** of the main body **10** of the inhaler **12** an open top **52** of the main body **10** forms an air inlet into the inhaler **12** communicating via air passageway **54** with the air outlet **46**, such that canister contents exiting nozzle **44** mix with air being sucked by the user through the air passageway **54** in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter **36** will now be described. The dose counter **36** includes an actuation pin **34** biased upwardly from underneath by a return spring **56** once installed in the main body **10**. As best shown in FIGS. **4**A, **6**H and **8**A, the pin **34** has side surfaces **58**, **60** arranged to slide between corresponding guide surfaces **62**, **64** located in a dose counter chamber **66** of the main body **10**, as well as an end stop surface **68** arranged to engage a corresponding end stop **70** formed in the dose counter chamber **66** to limit upward movement of the pin **34**. The pin **34** has a top part **72** which is circularly cylindrical and extends through an aperture **74** formed through a separator wall **76** which separates the canister chamber **18** from the dose counter chamber **66**. The top part **72** of the pin **34** has a flat top surface **78** which is arranged to engage the outer annular drive surface **32** of the canister **20**.

The actuation pin **34** is integrally formed with a drive or actuator pawl **80**. The actuator pawl **80** has a generally inverted U-shape configuration, having two mutually spaced and parallel arms **82**, **84** extending from a base portion of the actuation pin **34**, each holding at respective distal ends **88** thereof opposite ends of a pawl tooth member **90** which extends in a direction substantially perpendicular to the arms **82**, **84**, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth **92** of a ratchet wheel **94** of an incremental drive system **96** or ratchet mechanism **96** of the dose counter **36**. As shown for example in FIG. **10**B, the pawl tooth member **90** has a sharp lower longitudinal side edge **98** arranged to engage the drive teeth **92**, the edge-to-surface contact provided by this engagement

providing very accurate positioning of the actuator pawl **80** and resultant rotational positioning of the ratchet wheel **94**.

The dose counter **36** also has a chassis preassembly **100** which, as shown in FIGS. **4**A and **6**A, includes a chassis **102** having a first shaft **104** receiving the ratchet wheel **94** which is secured to a tape reel shaft **106**, and a second shaft (or split pin) **108** which is parallel to and spaced from the first shaft **104** and which slidably and rotationally receives a tape stock bobbin **110**.

As shown in FIG. **6**B, when the inhaler has not been used at all, the majority of a tape **112** is wound on the tape stock bobbin **110** and the tape **112** has a series of regularly spaced numbers **114** displayed therealong to indicate a number of remaining doses in the canister **20**. As the inhaler is repeatedly used, the ratchet wheel **94** is rotated by the actuator pawl **80** due to operation of the actuation pin **34** by the canister **20** and the tape **112** is incrementally and gradually wound on to the tape reel shaft **106** from the second shaft **108**. The tape **112** passes around a tape guide **116** of the chassis **102** enabling the numbers **114** to be displayed via a window **118** in a dose counter chamber cover **120** having a dose marker **132** formed or otherwise located thereon.

As shown in FIGS. **6**A and **6**D, the second shaft **108** is forked with two forks **124**, **126**. The forks **124**, **126** are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft **108** friction or control elements **128**, **130**, one on each fork. Each control element extends longitudinally along its respective fork **124**, **126** and has a longitudinally extending friction surface **132**, **134** which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore **136** inside the tape stock bobbin **110**. This control arrangement provided between the bore **136** and the control elements **128**, **130** provides good rotational control for the tape stock bobbin **110** such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin **110** and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. **6**D, as well as FIGS. **6**G and **10**A to **10**F, the chassis **102** is provided with an anti-back drive tooth **138** or count pawl **138** which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. **10**A to **10**F, when the actuation pin **34** is depressed fully so as to fire the metered valve (not shown) inside the canister **20**, the actuator pawl **80** pulls down on one of the teeth **92** of the ratchet wheel **94** and rotates the wheel **94** anticlockwise as shown in FIG. **6**D so as to jump one tooth **92** past the count pawl **138**, thereby winding the tape **112** a distance incrementally relative to the dose marker **122** on the dose counter chamber **120** so as to indicate that one dose has been used.

With reference to FIG. **10**B, the teeth of the ratchet wheel **94** have tips **143** which are radiused with a 0.1 mm radius between the flat surfaces **140**, **142**. The ratchet wheel **94** has a central axis **145** which is 0.11 mm above datum plane **220** (FIG. **9**). A top/nose surface **147** of the anti-back drive tooth **138** is located 0.36 mm above the datum plane **220**. The distance vertically (i.e. transverse to datum plane **220**—FIG. **9**) between the top nose surface **147** of the anti-back drive tooth is 0.25 mm from the central axis **145** of the wheel **94**. Bump surface **144** has a lateral extent of 0.20 mm, with a vertical length of a flat **145'** thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis **145**), the top **149** of the bump surface **144** being 3.02 mm vertically below the axis **145**, and the flat **145'** being spaced a distance sideways (i.e. parallel to the datum plane **220**) 2.48 mm from the axis **145**. The top surface **78** of the pin **34** (FIG. **6**H) is 11.20 mm above the datum plane **220** (FIG. **9**) when the actuator pawl **80** and pin **34** are in the start configuration. The length of the valve stem **22** is 11.39 mm and the drive surface **32** of the canister **20** is 11.39 mm above the datum plane **220** when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister **20** and the pin **34** in this configuration.

FIGS. **10**A and **10**B show the actuator pawl **80** and ratchet wheel **94** and count pawl **138** in a start position in which the flat top **78** of the pin **34** has not yet been engaged by the outer annular drive surface **32** of the canister **20** or at least has not been pushed down during a canister depression.

In this "start" position, the count pawl **138** engages on a non-return back surface **140** of one of the teeth **92** of the ratchet wheel **94**. The lower side edge **98** of the actuator pawl is a distance "D" (FIG. **9**) 1.33 mm above datum plane **220** which passes through bottom surface or shoulder **41** of valve stem block **40**, the datum plane **220** being perpendicular to a main axis "X" of the main body **10** of the inhaler **12** which is coaxial with the centre of the valve stem block bore **43** and parallel to a direction of sliding of the canister **20** in the main body **10** of the inhaler **12** when the canister is fired.

As shown in FIG. **10**B, an advantageous feature of the construction is that the pawl tooth/actuator **90** acts as a supplementary anti-back drive member when the inhaler **12** is not being used for inhalation. In particular, if the inhaler **12** is accidentally dropped, resulting in a jolt to the dose counter **36** then, if the wheel **94** would try to rotate clockwise (backwards) as shown in FIG. **10**B, the back surface **140** of a tooth will engage and be blocked by the tooth member **90** of the pawl **80**. Therefore, even if the anti-back drive tooth **138** is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel **94** is prevented and, upon the next canister firing sequence, the pawl **90** will force the wheel **94** to catch up to its correct position so that the dose counter **36** continues to provide correct dosage indication.

FIG. **10**C shows a configuration in which the actuator pawl **80** has been depressed with the pin **34** by the canister **20** to a position in which the side edge **98** of the pawl tooth member **90** is just engaged with one of the teeth **92** and will therefore upon any further depression of the pin **34** begin to rotate the wheel **94**. This is referred to as a "Reset" position or configuration. In this configuration, the lower side edge **98** of the actuator **80** is 0.64 mm above the datum plane **220**.

FIG. **10**D shows a configuration in which the actuator pawl **80** has been moved to a position lower than that shown in FIG. **10**C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle **44**. It will be noted that in this configuration the count pawl **138** is very slightly spaced from the back surface **140** of the same tooth **92** that it was engaging in the configuration of FIG. **10**D. The configuration shown in FIG. **10**D is known as a "Fire" configuration. In this configuration the lower side edge **98** of the actuator **80** is 0.47 mm below the datum plane **220**.

FIG. **10**E shows a further step in the sequence, called a "Count" position in which the actuator pawl **80** has rotated the ratchet wheel **94** by the distance circumferentially angularly between two of the teeth **92**, such that the count pawl **138** has just finished riding along a forward surface **142** of one of the teeth **92** and has resiliently jumped over the tooth into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently

long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than one in 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10**F, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6**G) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10**F will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10**F.

As shown in FIGS. **7**C and **7**D, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7**B a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7**A and schematically in FIG. **7**B, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** a as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **144**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7**C for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8**A, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8**B, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4**B, **4**C and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6**B) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6**B may as shown in FIG. **8**C be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8**D, the dose counter chamber cover **120** may be fitted over the dose

counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8**D being "200", thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8**D, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18**C and **19**C, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6**F. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radio extent of the control elements **128**, **130**, is 3.1 millimeters and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18**C and **19**C is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18**A to **18**C when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19**A to **19**C, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**

It will be appreciated that whereas FIGS. **18**B and **19**B are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18**A and **19**A are cross-sections. FIG. **19**A is a section on the plane A-A' in FIG. **19**C and FIG. **18**A is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

As the inhaler **12** is used and the ratchet wheel **94** rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin **108** at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin **108** at such rotational positions and this may involve a click forward of the stock bobbin **110** to the next position equivalent to that in FIGS. **19**A to **19**C in which the control elements **128**, **130** of the split pin art located in the concavities **302**. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape **112** from loosening during transit if the inhaler **12** is dropped, such as onto a hard surface. This is highly advantageous, since the tape **11** is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. **18**C and **19**C, the forks **124**, **126** rotate about a point **316** on the split pin where the forks **124**, **126** come together. This rotational action means that there is a camming action between the forks **124**, **126** and the engagement surface **300** without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface **300** and forks **124**, **126** are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler **12** is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape **112** to overcome the regulator at the stock bobbin **110**. 0.32 N is achieved with the control elements **128** having the profile shown in FIG. **19**C and 0.38 N is achieved with the profile of the control elements **128** altered to be as shown as described with reference to FIG. **6**F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. **15** to **20** does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape **112** as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape **112** can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities **302** and convex wall portions **304**, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements **128**, **130** are provided, so that all of the control elements **128**, **130** will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface **300** on the inside of the stock bobbin **110**, it could be placed on the outside of the stock bobbin **110** so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface **300** and forks **124**, **126** does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel **94**. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin **110** can be wound backwards during or after fitting the bobbin **100**, shaft **106** and tape **112** onto the carriage **102**, if desired.

The stock bobbin **110** and the carriage **102** including the split pin **108** are both moulded of polypropylene material.

It will be seen from FIG. **16** that the cross-sectional shape **301** is not symmetrical within the hexagonal socket **204**. This has enabled the hexagonal socket **204** to be maintained at a useful size while still allowing the desired size and geometry of the cross section **301** to fit without interfering with the hexagonal shape of the hexagonal socket **204** and also permits moulding to work during manufacture.

As shown in FIG. **17**, the stock bobbin **110** has a series of four circumferential ribs **330** inside it and a spaced thereabout. These hold the stock bobbin **110** on the correct side of the mould tool during moulding.

FIGS. **21** and **22** show a preferred embodiment in accordance with the invention of an inhaler **510** for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler **510** is as disclosed in FIGS. **1** to **16** or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin **110** and second shaft **108** of the dose counter **516** modified so as to be as in FIGS. **15** to **20** hereof. Thus, the dry powder inhaler **510** generally includes a housing **518**, and an assembly **512** received in the housing (see FIG. **21**). The housing **518** includes a case **520** having an open end **522** and a mouthpiece **524** (FIG. **25**) for patient inhalation, a cap **526** secured to and closing the open end **522** of the case **520**, and a cover **528** pivotally mounted to the case **520** for covering the mouthpiece **524**. As shown in FIG. **22**, the inhaler **510** also includes an actuation spring **569**, first yoke **566** with opening **572**, bellows **540** with crown **574**, a reservoir **514**, second yoke **568** with hopper **542** and dose counter **516** mounted thereto, and case **520** has transparent window **5130** thereon for viewing dose counter tape indicia **5128**. The dose metering system also includes two cams **570** mounted on the mouthpiece cover **528** and movable with the cover **528** between open and closed positions. The cams **570** each include an opening **580** for allowing outwardly extending hinges **582** of the case **520** to pass therethrough and be received in first recesses **584** of the cover **528**. The cams **570** also include bosses **586** extending outwardly and received in second recesses **588** of the cover **528**, such that the cover **528** pivots about the hinges **582** and the cams **570** move with the cover **528** about the hinges **582**. As described in EP-A-1330280, cams **570** act upon cam followers **578** to move second yoke **568** up and down and thereby operate dose counter by engagement of pawl **5138** on the second yoke **568** with teeth **5136**. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system **516** therefore includes a ribbon or tape **5128** (FIGS. **23** & **24**), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window **5130** provided in the housing **18** (see FIG. **22**). The dose counting system **516** includes the rotatable stock bobbin **110** (as described above), an indexing spool **5134** rotatable in a single direction, and the ribbon **5128** rolled and received on the bobbin **110** and having a first end **5127** secured to the spool **5134**, wherein the ribbon **5128** unrolls from the bobbin **110** so that the indicia are successively displayed as the spool **5134** is rotated or advanced. In FIGS. **23** and **24** the wavelike engagement surface **300** of the bobbin **110** is not shown for the purposes of clarity.

The spool **134** is arranged to rotate upon movement of the yokes **566**, **568** to effect delivery of a dose of medicament from reservoir **514**, such that the number on the ribbon **5128** is advanced to indicate that another dose has been dispensed by the inhaler **510**. The ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase or

decrease upon rotation of the spool **5134**. For example, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool **5134** to indicate the number of doses remaining in the inhaler **510**. Alternatively, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool **5134** to indicate the number of doses dispensed by the inhaler **10**.

The indexing spool **5134** includes radially extending teeth **5136**, which are engaged by pawl **5138** extending from a cam follower **578** of the second yoke **568** upon movement of the yoke to rotate, or advance, the indexing spool **5134**. More particularly, the pawl **5138** is shaped and arranged such that it engages the teeth **5136** and advances the indexing spool **5134** only upon the mouthpiece cover **528** being closed and the yokes **566**, **568** moved back towards the cap **526** of the housing **518**.

The dose counting system **516** also includes a chassis **5140** that secures the dose counting system to the hopper **542** and includes shafts **108**, **5144** for receiving the bobbin **110** and the indexing spool **5134**. As described above with reference to FIGS. **1** to **20**, the bobbin shaft **108** is forked and includes radially nubs **5146** for creating a resilient resistance to rotation of the bobbin **110** on the shaft **108** by engaging with the wavelike engagement surface **300** inside the bobbin **110**. A clutch spring **5148** is received on the end of the indexing spool **5134** and locked to the chassis **5140** to allow rotation of the spool **5134** in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed:

1. An inhaler for metered dose inhalation, the inhaler comprising:

a main body having a canister housing,

a medicament canister, which is moveable relative to the canister housing and retained in a central outlet port of the canister housing arranged to mate with a canister fire stem of the medicament canister, and

a dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of the medicament canister,

wherein the canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall, and

wherein the canister housing has a longitudinal axis X which passes through the center of the central outlet port,

the inner wall canister support formation, the actuation member, and the central outlet port lying in a common plane coincident with the longitudinal axis X.

2. The inhaler as claimed in claim **1** wherein the medicament canister is movable relative to the dose counter.

3. The inhaler as claimed in claim **1** further comprising an aperture formed in the inner wall through which the portion of the actuation member extends.

4. The inhaler as claimed in claim **1**, wherein the first inner wall canister support formation comprises a support rail which extends longitudinally along an inside surface of the main body.

5. The inhaler as claimed in claim **4**, wherein the support rail includes a step formed thereon.

6. The inhaler as claimed in claim **4** further comprising a plurality of support rails each of which extends longitudinally along an inside surface of the main body.

7. The inhaler as claimed in claim **6**, wherein two of the plurality of support rails are positioned at opposite ends of the inside surface of the main body to face each other.

8. The inhaler as claimed in claim **4**, wherein the support rail includes two steps formed thereon, the steps being spaced apart longitudinally along an inside surface of the main body.

9. The inhaler as claimed in claim **4**, wherein the support rail merges with the inner wall at a location adjacent the aperture.

10. The inhaler as claimed in claim **9**, wherein a width dimension of the support rail is not constant, and the width dimension is greatest at the location where the support rail merges with the inner wall.

* * * * *

Exhibit C

US009808587B2

(12) **United States Patent**
Walsh et al.

(10) **Patent No.: US 9,808,587 B2**
(45) **Date of Patent: *Nov. 7, 2017**

(54) **DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR**

(71) Applicants: **IVAX PHARMACEUTICALS IRELAND**, Waterford (IE); **NORTON (WATERFORD) LIMITED**, Waterford (IE); **TEVA PHARMACEUTICALS IRELAND**, Waterford (IE)

(72) Inventors: **Declan Walsh**, Co. Kilkenny (IE); **Derek Fenlon**, Co. Wexford (IE); **Simon Kaar**, Co. Cork (IE); **Jan Geert Hazenberg**, Co. Kilkenny (IE); **Daniel Buck**, Co. Waterford (IE); **Paul Clancy**, Waterford (IE); **Robert Charles Uschold**, Leominster, MA (US); **Jeffrey A. Karg**, Hopkinton, MA (US)

(73) Assignees: **IVAX PHARMACEUTICALS IRELAND** (IE); **TEVA PHARMECUTICALS IRELAND** (IE); **NORTON (WATERFORD) LIMITED** (IE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/269,249**

(22) Filed: **Sep. 19, 2016**

(65) **Prior Publication Data**

US 2017/0000962 A1 Jan. 5, 2017

Related U.S. Application Data

(60) Continuation of application No. 14/103,324, filed on Dec. 11, 2013, now Pat. No. 9,463,289, which is a (Continued)

(51) **Int. Cl.**
G06M 1/06 (2006.01)
A61M 11/00 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61M 15/0078*** (2014.02); ***A61M 11/00*** (2013.01); ***A61M 15/009*** (2013.01);
(Continued)

(58) **Field of Classification Search**
USPC 235/8, 103; 128/200.23
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,174,890 A 11/1979 Johnson
4,669,838 A 6/1987 Hibbard
(Continued)

FOREIGN PATENT DOCUMENTS

CA 2501726 9/2006
EP 1330280 7/2003
(Continued)

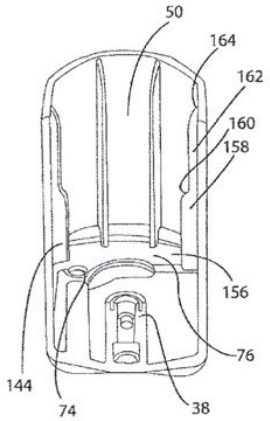
OTHER PUBLICATIONS

Final Office Action dated Oct. 20, 2016 for U.S. Appl. No. 14/699,567.
(Continued)

Primary Examiner — Daniel Hess
(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP

(57) **ABSTRACT**

An inhaler includes a main body having a canister housing, a medicament canister retained in a central outlet port of the canister housing, and a dose counter having an actuation member for operation by movement of the medicament canister. The canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall. The canister housing
(Continued)



has a longitudinal axis X which passes through the center of the central outlet port. The first inner wall canister support formation, the actuation member, and the central outlet port lie in a common plane coincident with the longitudinal axis X such that the first inner wall canister support formation protects against unwanted actuation of the dose counter by reducing rocking of the medicament canister relative to the main body of the inhaler.

22 Claims, 17 Drawing Sheets

Related U.S. Application Data

division of application No. 13/110,532, filed on May 18, 2011, now Pat. No. 8,978,966.

(60) Provisional application No. 61/417,659, filed on Nov. 29, 2010, provisional application No. 61/345,763, filed on May 18, 2010.

(51) **Int. Cl.**
A61M 15/00 (2006.01)
G06M 1/24 (2006.01)

(52) **U.S. Cl.**
CPC ***A61M 15/0025*** (2014.02); ***A61M 15/0026*** (2014.02); ***A61M 15/0065*** (2013.01); ***A61M 15/0071*** (2014.02); ***G06M 1/246*** (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,687,359	A	8/1987	Barrus	
5,482,030	A	1/1996	Klein	
5,861,911	A	1/1999	Oosaka	
6,446,627	B1	9/2002	Bowman	
6,718,972	B2	4/2004	OLeary	
8,418,690	B2	4/2013	Power	
8,474,448	B2	7/2013	Oi	
8,978,966	B2	3/2015	Walsh et al.	
9,174,013	B2	11/2015	Walsh et al.	
9,463,289	B2 *	10/2016	Walsh	A61M 15/0065
2002/0047021	A1	4/2002	Blacker	
2002/0078949	A1	6/2002	OLeary	
2002/0078950	A1	6/2002	OLeary	
2002/0084891	A1	7/2002	Mankins et al.	
2003/0209239	A1	11/2003	Rand	
2004/0089298	A1	5/2004	Haikarainen et al.	
2004/0095746	A1	5/2004	Murphy	
2005/0028815	A1	2/2005	Deaton	
2005/0087191	A1 *	4/2005	Morton	A61M 15/0065 128/205.23
2006/0096594	A1	5/2006	Bonney	
2006/0107949	A1 *	5/2006	Davies	A61M 15/0065 128/200.23
2006/0107979	A1	5/2006	Kim	
2007/0062518	A1	3/2007	Geser	
2008/0242465	A1	10/2008	Strobel	
2009/0178678	A1	7/2009	OLeary	
2010/0089395	A1	4/2010	Power	
2010/0218759	A1	9/2010	Anderson	
2011/0041845	A1	2/2011	Solomon	
2012/0006322	A1	1/2012	Anderson	

FOREIGN PATENT DOCUMENTS

EP	1486227		12/2004
GB	2320489		6/1998
IL	201256		11/2014
JP	02502129		7/1990
JP	450059		8/1992
JP	07100205		4/1995
JP	10504220		4/1998
JP	2002528144		9/2002
JP	2004501685		1/2004
JP	2008-94103	A	4/2008
JP	2008094103		4/2008
JP	2008261423		10/2008
JP	2009233308		10/2009
JP	2009257392		11/2009
JP	2010096308		4/2010
WO	8909078		10/1989
WO	9628205		9/1996
WO	9828033		7/1998
WO	9936115		7/1999
WO	02/00281	A2	1/2002
WO	03101514		12/2003
WO	2005102430		11/2005
WO	2006062449		6/2006
WO	2006062449	A1	6/2006
WO	2007012861		2/2007
WO	2007062518		6/2007
WO	2008023019		2/2008
WO	2008119552		2/2008
WO	2011012325		2/2011
WO	2011012327		2/2011

OTHER PUBLICATIONS

Advisory Action dated Mar. 13, 2017 for U.S. Appl. No. 14/699,567.
Non-Final Office Action dated Jan. 12, 2017 for U.S. Appl. No. 14/713,620, 8 pages.
Final Rejection dated Sep. 27, 2016 for U.S. Appl. No. 14/699,578.
Final Office Action dated Aug. 31, 2016 for U.S. Appl. No. 14/713,620, 7 pages.
Advisory action dated Feb. 9, 2017 for U.S. Appl. No. 14/699,584.
Non-final rejection dated Jul. 12, 2016 for U.S. Appl. No. 14/713,643.
File History for U.S. Appl. No. 15/271,738.
File History for U.S. Appl. No. 15/269,102.
File History for U.S. Appl. No. 15/262,818.
File History for U.S. Appl. No. 15/289,553.
File History for U.S. Appl. No. 15/269,249.
Final rejection dated Oct. 20, 2016 or U.S. Appl. No. 14/699,584.
Non-Final Office Action dated Jun. 24, 2016 for U.S. Appl. No. 14/713,620, 7 pages.
Final rejection dated Oct. 20, 2016 or U.S. Appl. No. 14/713,631.
Advisory Action dated Mar. 16, 2017 or U.S. Appl. No. 14/713,633.
Entire patent prosecution history of U.S. Appl. No. 13/110,532, filed May 18, 2011, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,324, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,343, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,353, filed Dec. 11, 2013, entitled,"Dose Counters for Inhalers, Inhalers and Methods of Ass Embly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,363, filed Dec. 1, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,392, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".

(56) **References Cited**

OTHER PUBLICATIONS

Entire patent prosecution history of U.S. Appl. No. 14/699,567, filed Apr. 29, 2015, entitled, "Dose Counter for Inhaler and Method for Counting Doses.".
Entire patent prosecution history of U.S. Appl. No. 14/699,578, filed Apr. 29, 2015, entitled, "Dose Counter for Inhaler Having a Bore !and Shaft Arrangement.".
Entire patent prosecution history of U.S. Appl. No. 14/699,584, filed Apr. 29, 2015, entitled, "Dose Counter for Inhaler Having an Antireverse Rotation Actuator.".
Entire patent prosecution history of U.S. Appl. No., 14/713,612, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/713,620, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/713,643, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
European Patent Office Communication, dated Apr. 24, 2014 of counterpart European Patent Application No. 11 010 211.8.
European Patent Office Communication, dated Apr. 24, 2014 of counterpart European Patent Application No. 11 010 212.6.
First Examination Report of counterpart New Zealand Patent Application No. 603466, dated Jul. 1, 2013.
Office Action issued by the Israel Patent Office on Jul. 3, 2017 in reference to Israel Patent Application No. 247396, 3 pages.
Office Action issued by the Israel Patent Office on Jul. 27, 2017 in reference to Israel Patent Application No. 247402, 4 pages.

* cited by examiner

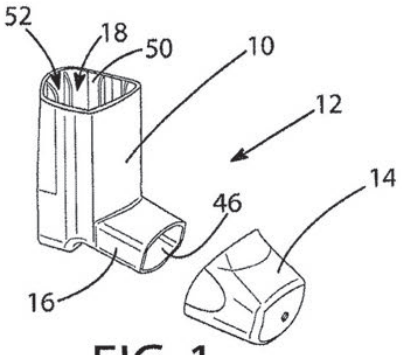


FIG. 1

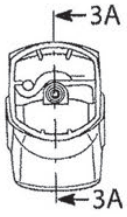


FIG. 2

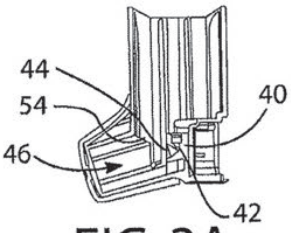


FIG. 3A

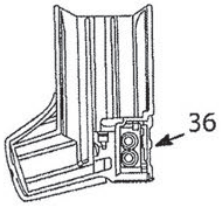


FIG. 3B

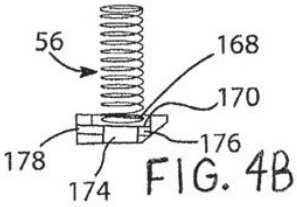


FIG. 4B

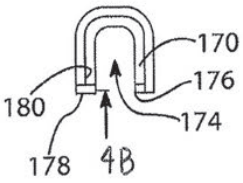


FIG. 4C

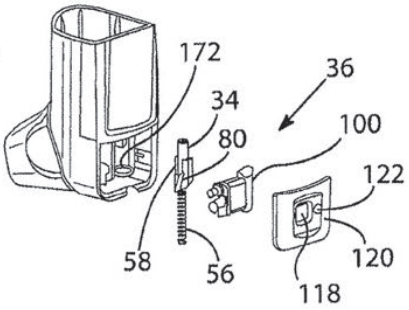


FIG. 4A

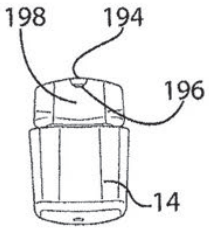


FIG. 5

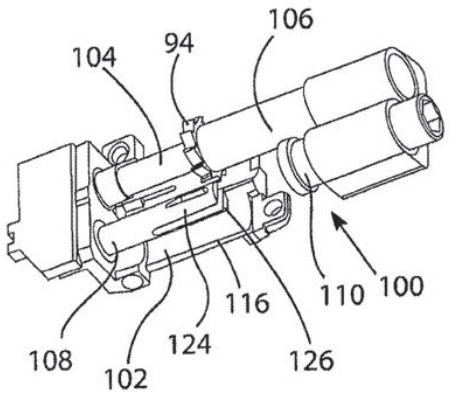


FIG. 6A

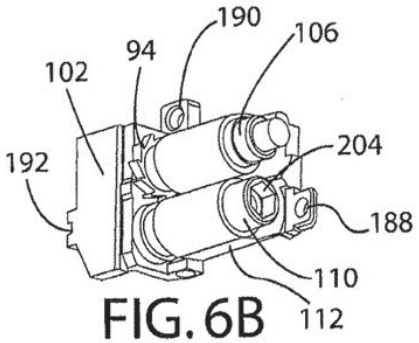


FIG. 6B

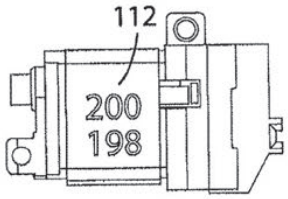


FIG. 6C

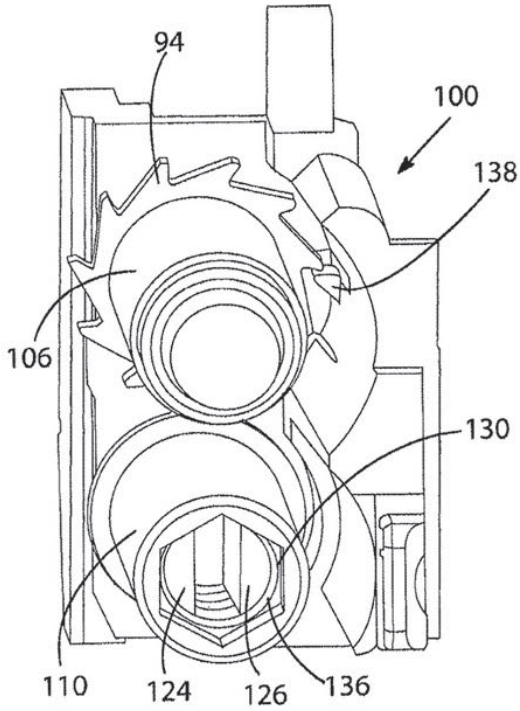


FIG. 6D

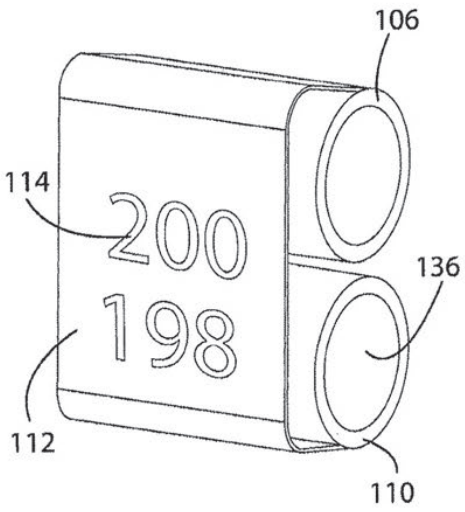


FIG. 6E

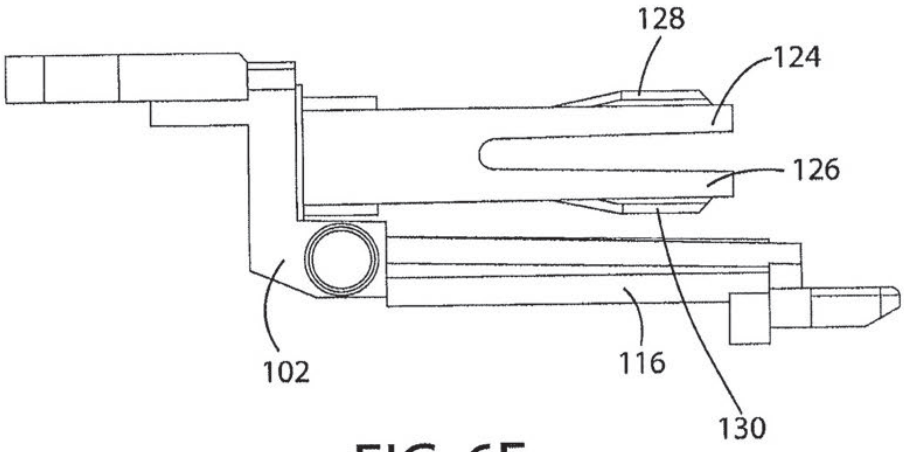


FIG. 6F

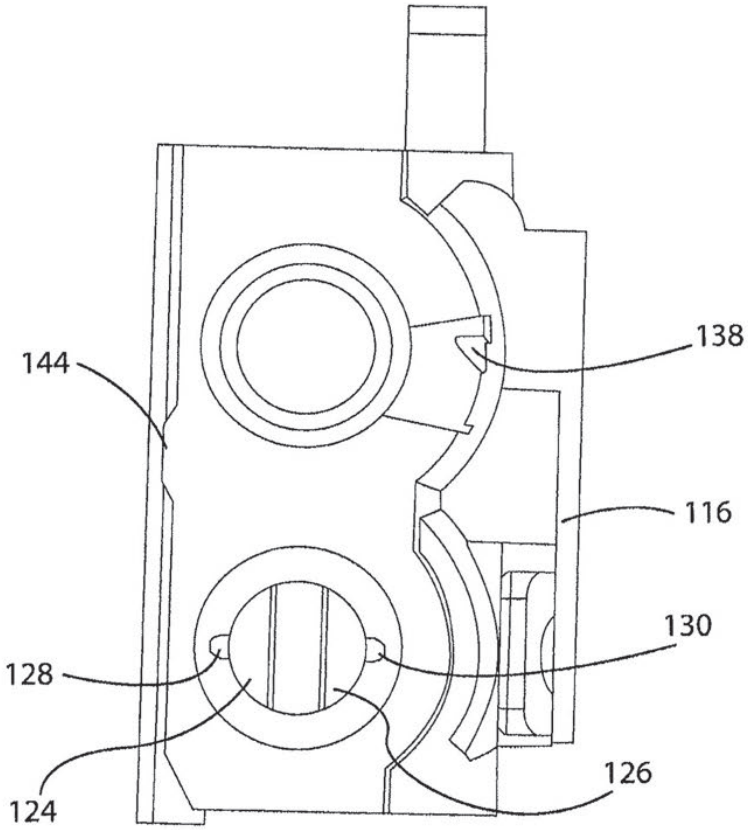


FIG. 6G

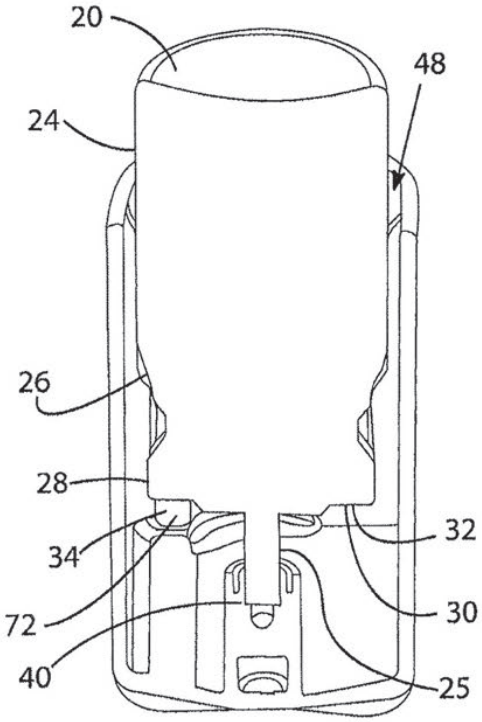


FIG. 7A

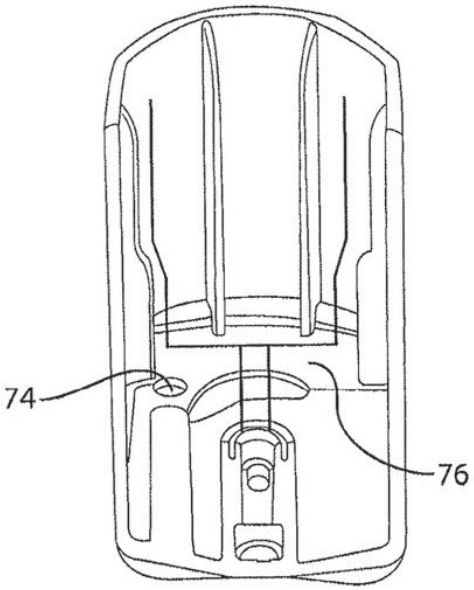


FIG. 7B

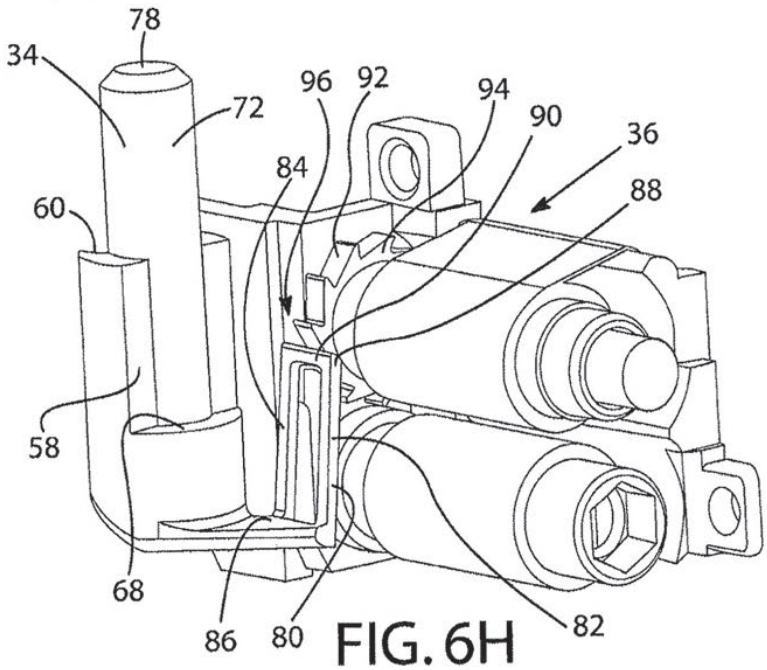


FIG. 6H

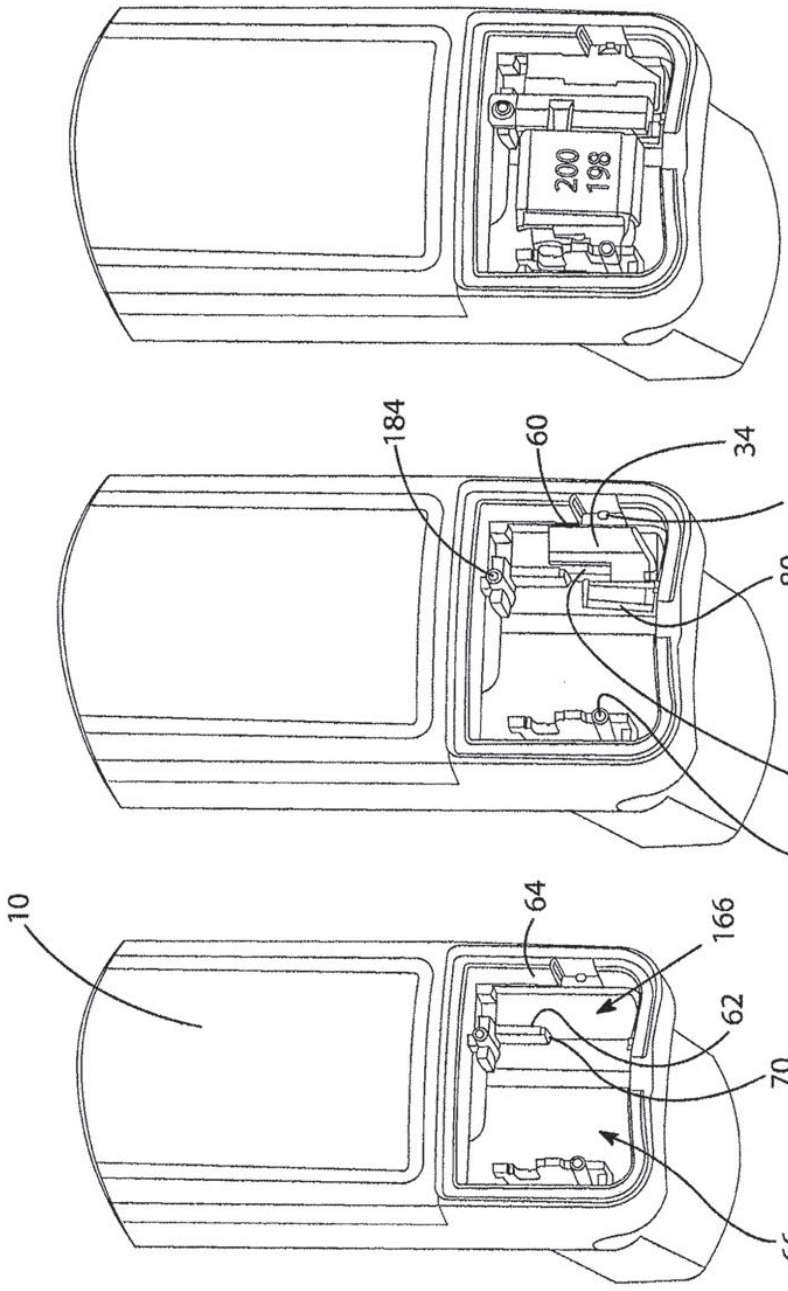


FIG. 8C

FIG. 8B

FIG. 8A

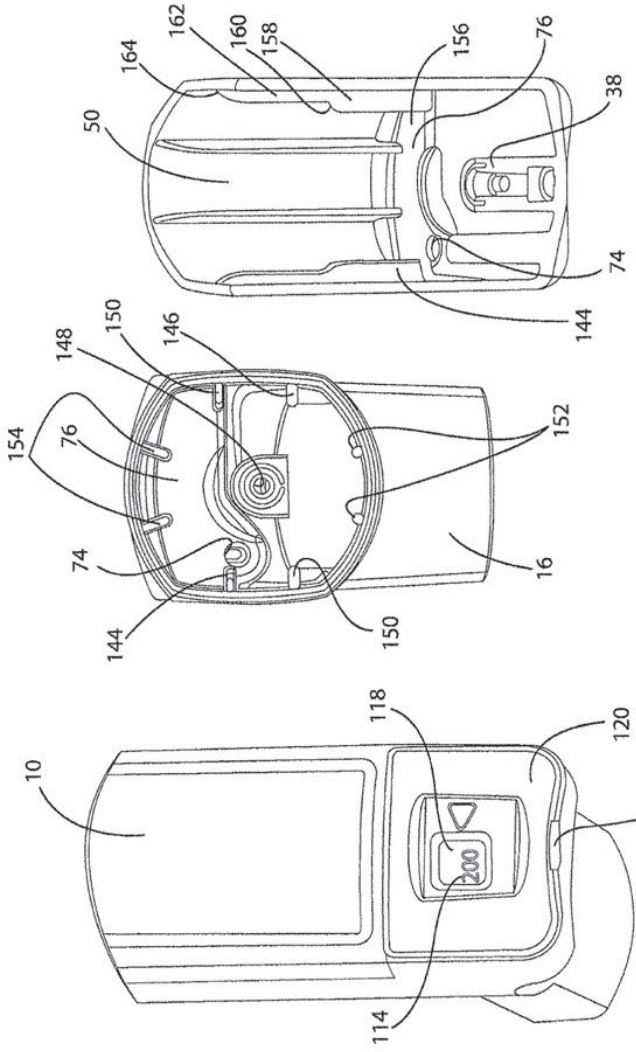


FIG. 7C

FIG. 7D

FIG. 8D

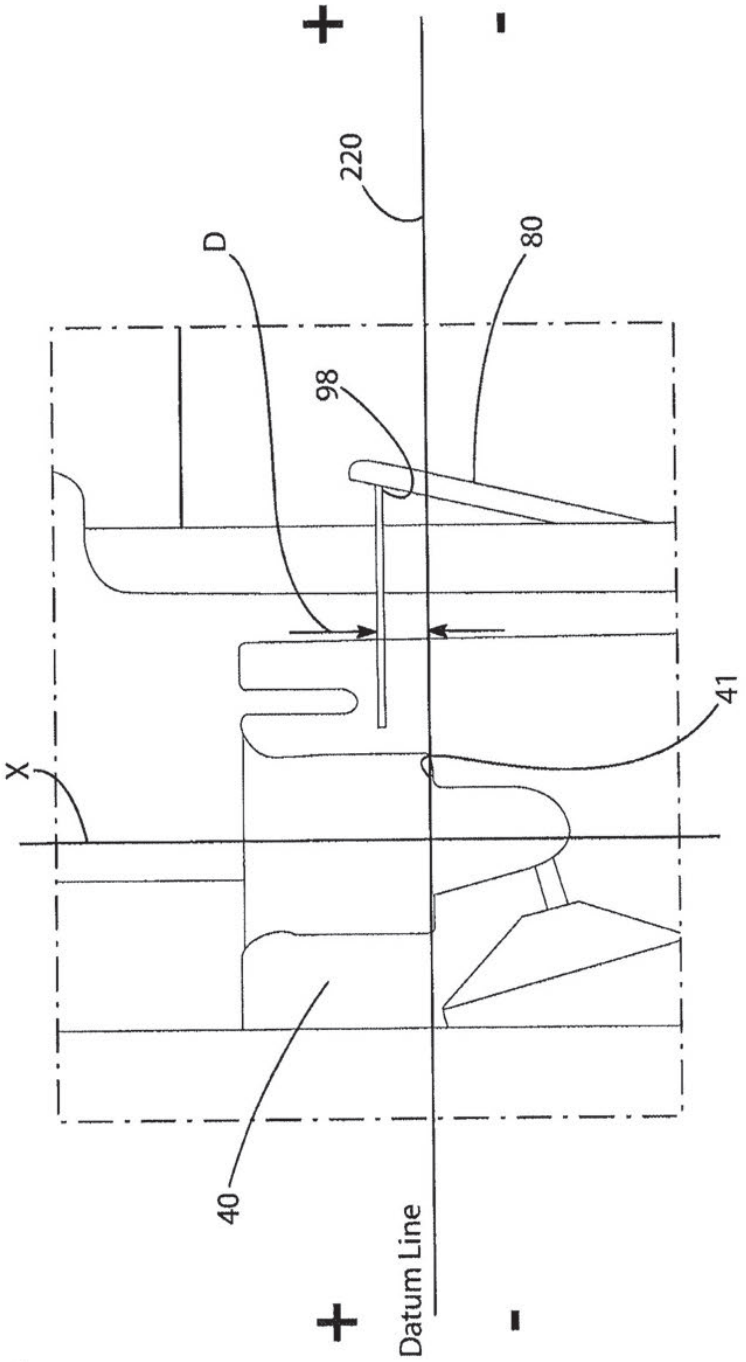


FIG. 9

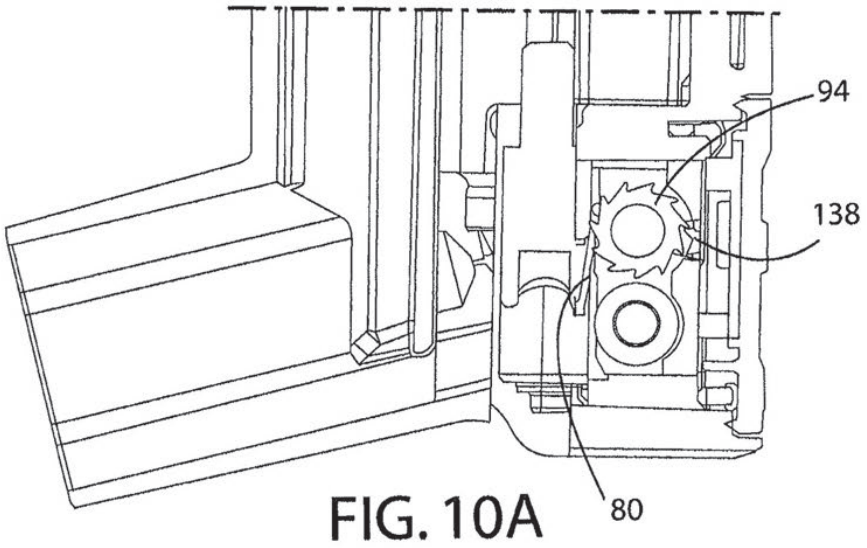


FIG. 10A

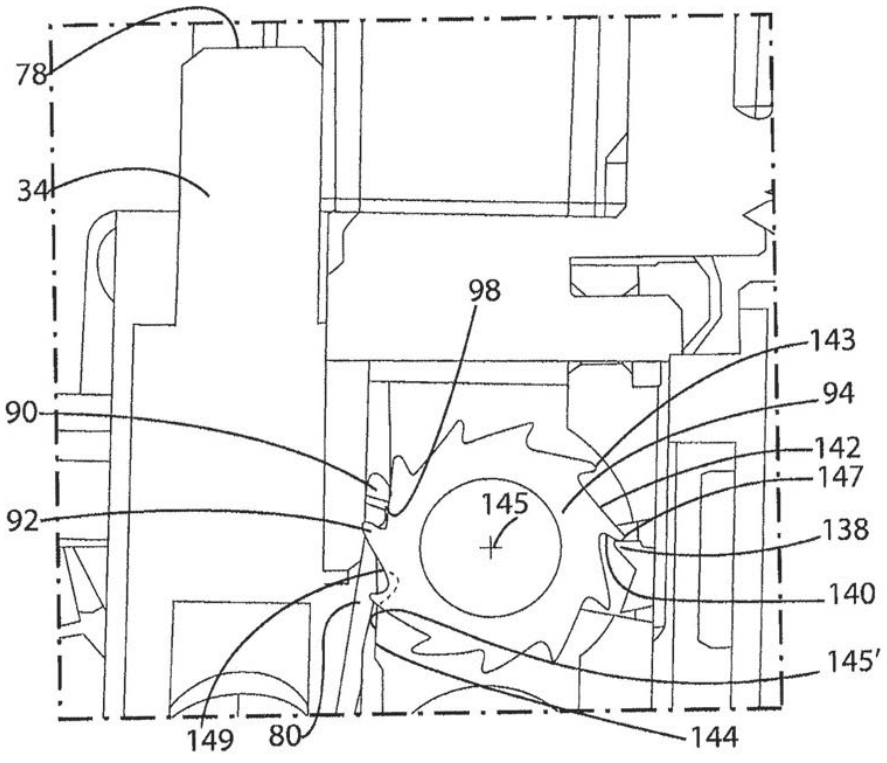


FIG. 10B

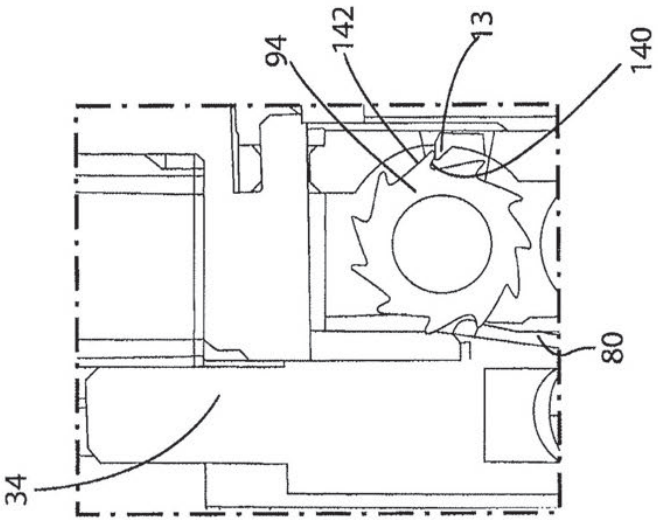


FIG. 10E

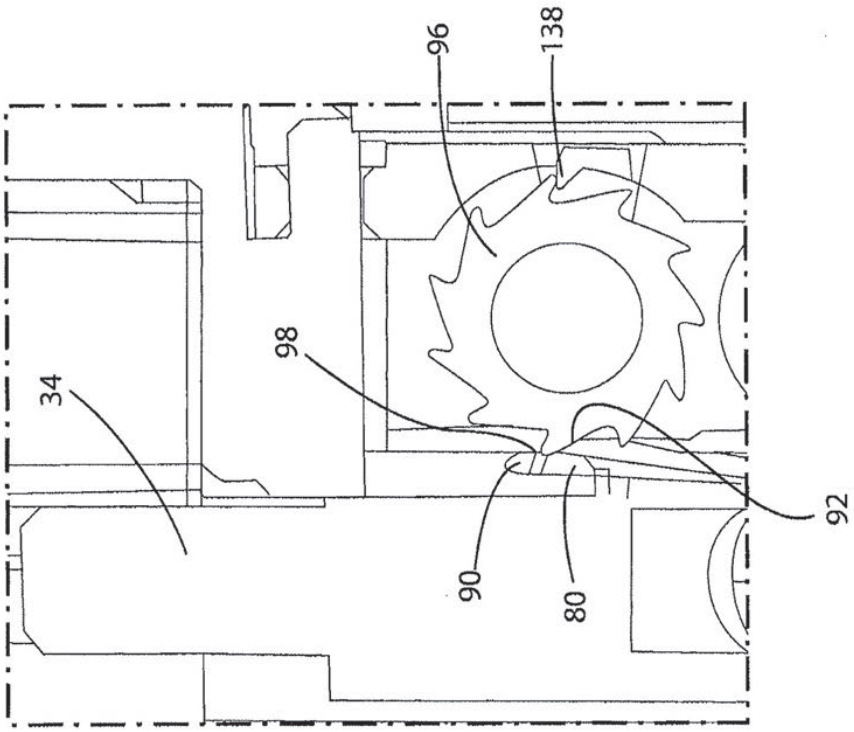


FIG. 10C

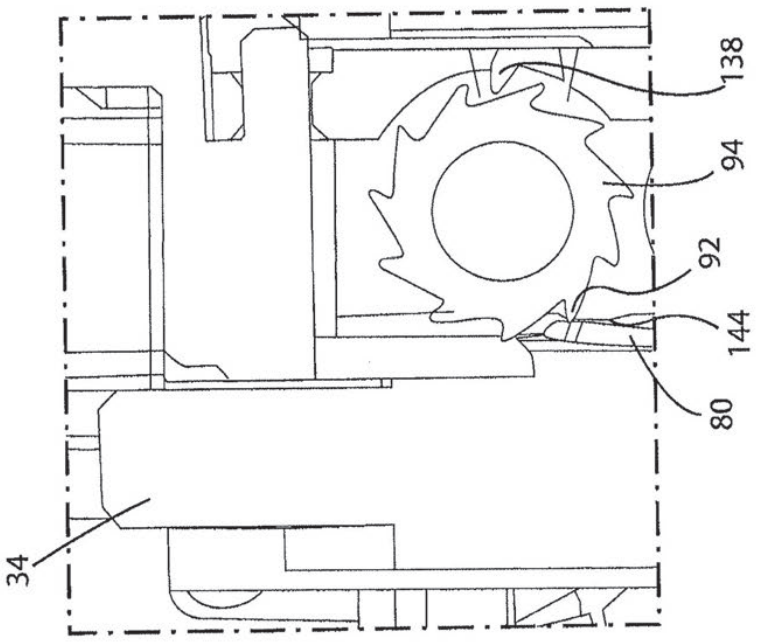


FIG. 10F

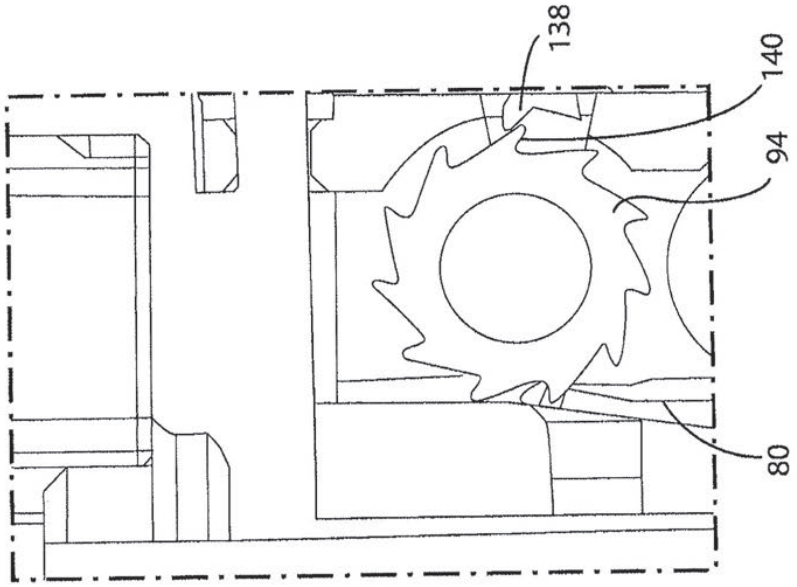


FIG. 10D

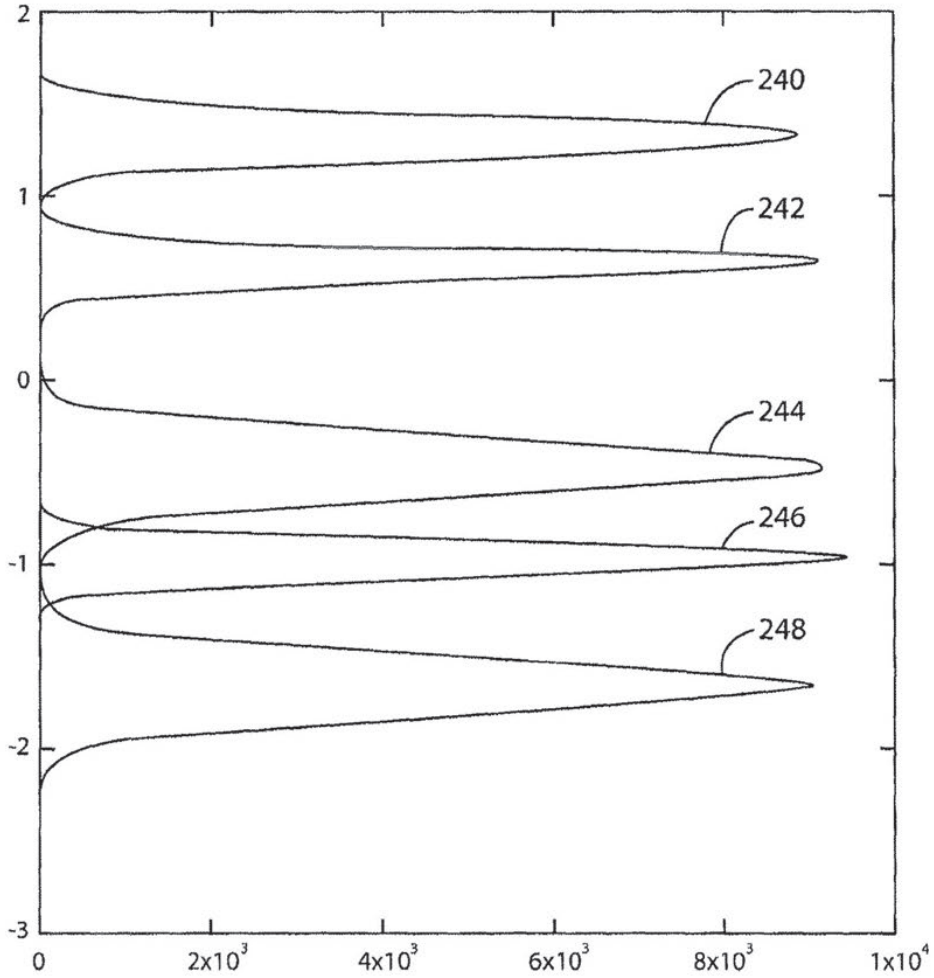

2
1
0
-1
-2
-3
0
2x10^3
4x10^3
6x10^3
8x10^3
1x10^4
240
242
244
246
248

FIG. 11

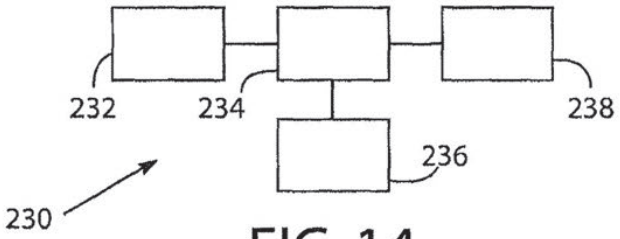

232
234
238
236
230

FIG. 14

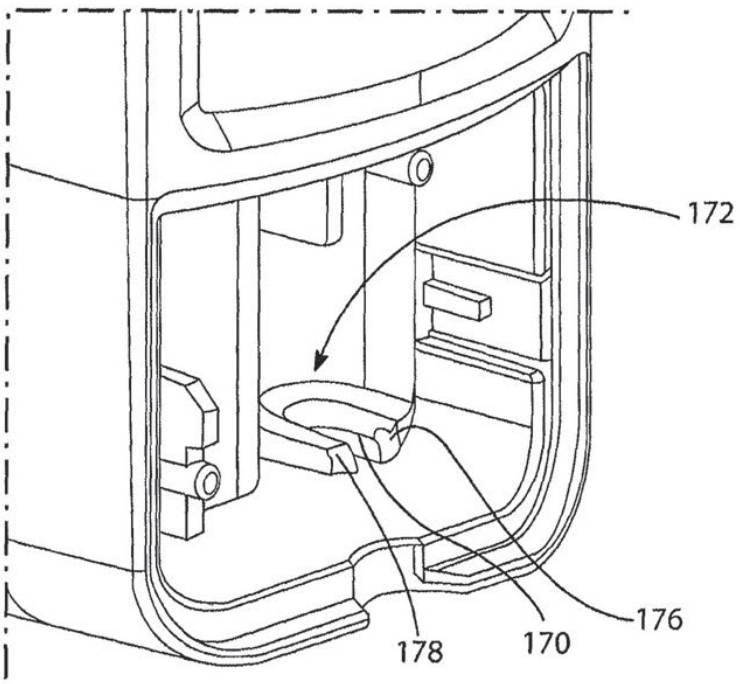
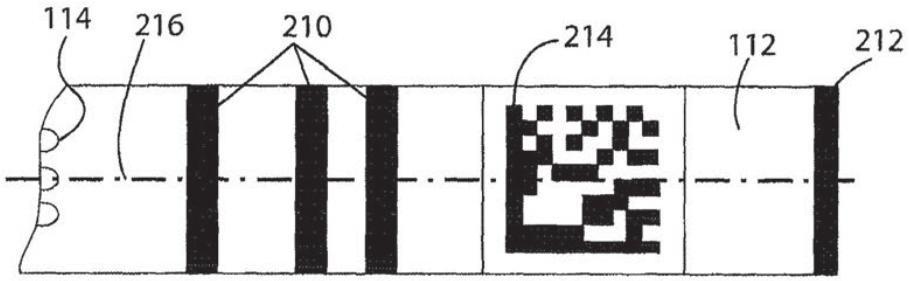


FIG. 12



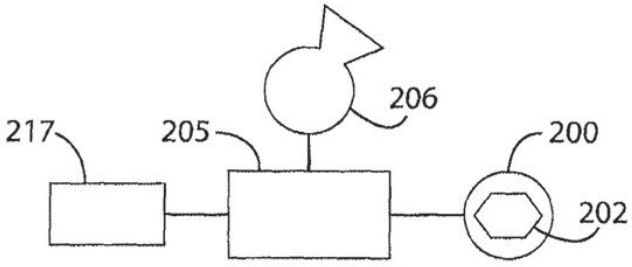


FIG. 13

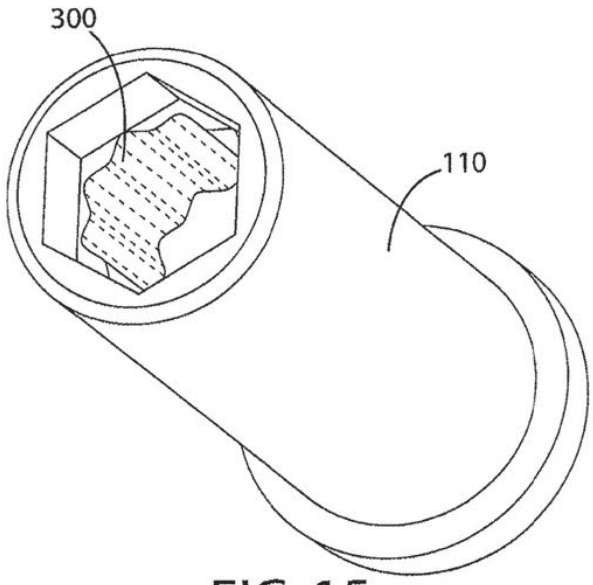


FIG. 15

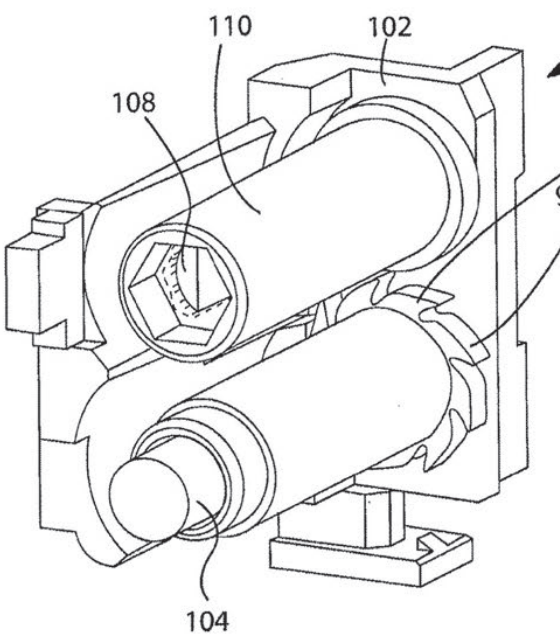


FIG. 20

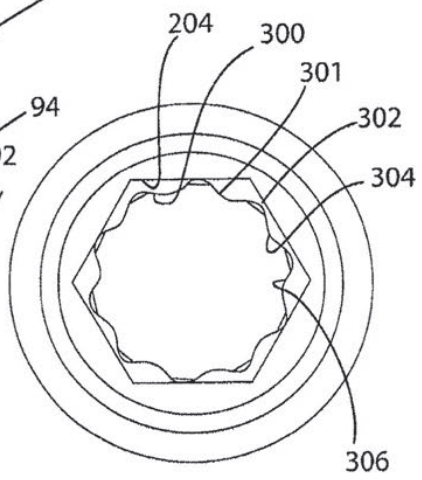


FIG. 16

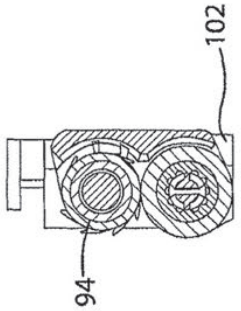


FIG. 19A

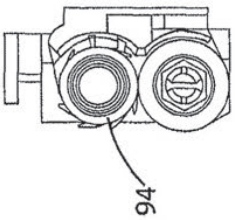


FIG. 19B

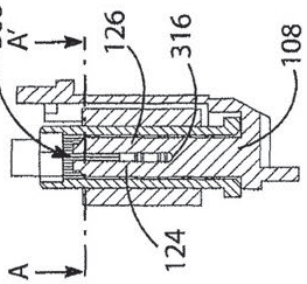


FIG. 19C

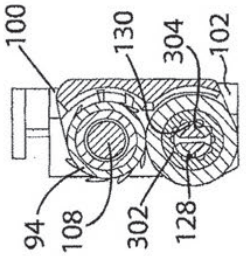


FIG. 18A

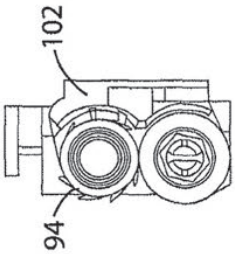


FIG. 18B

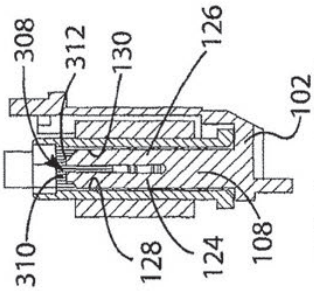


FIG. 18C

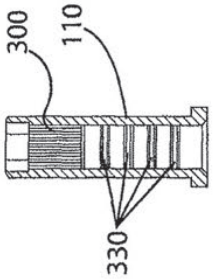


FIG. 17

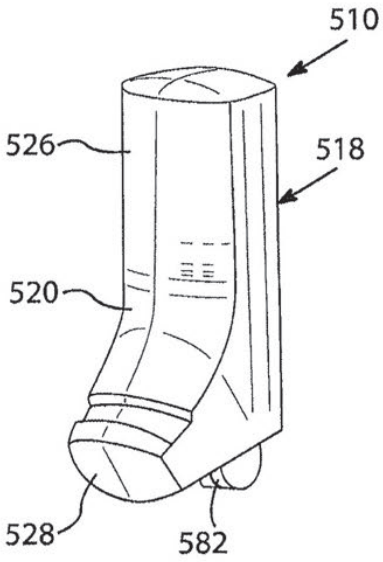

510
526
518
520
528
582

FIG. 21

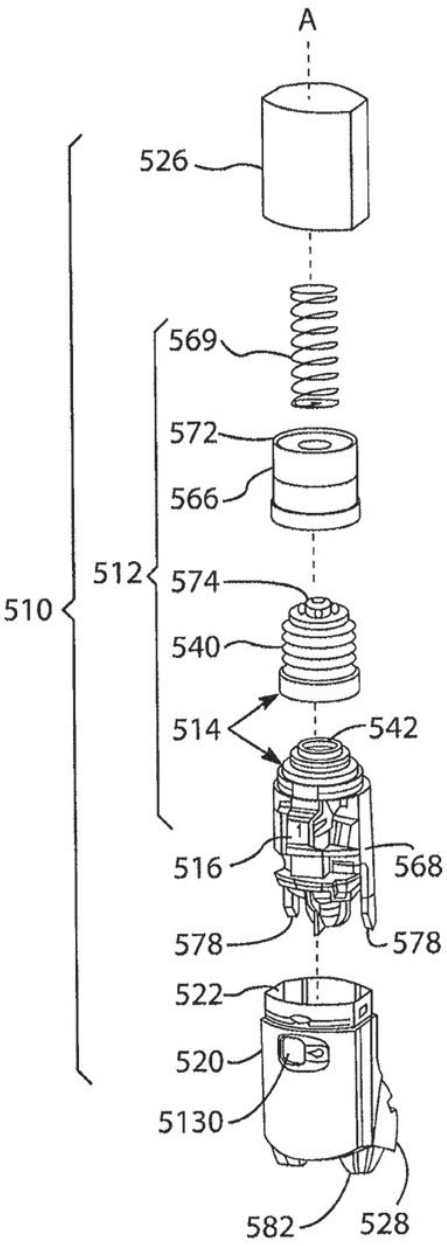

A
526
569
572
566
512
574
510
540
514
542
516
568
578
578
522
520
5130
582
528

FIG. 22

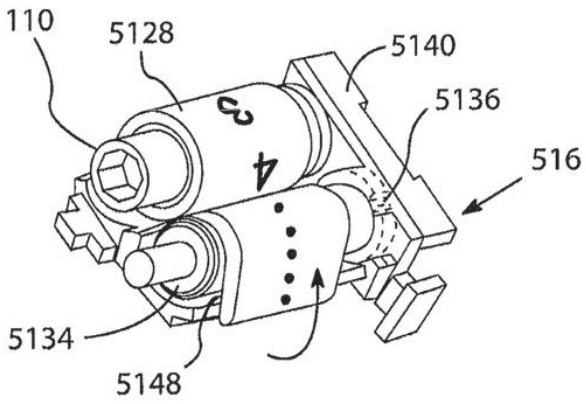

110
5128
5140
5136
516
5134
5148

FIG. 23

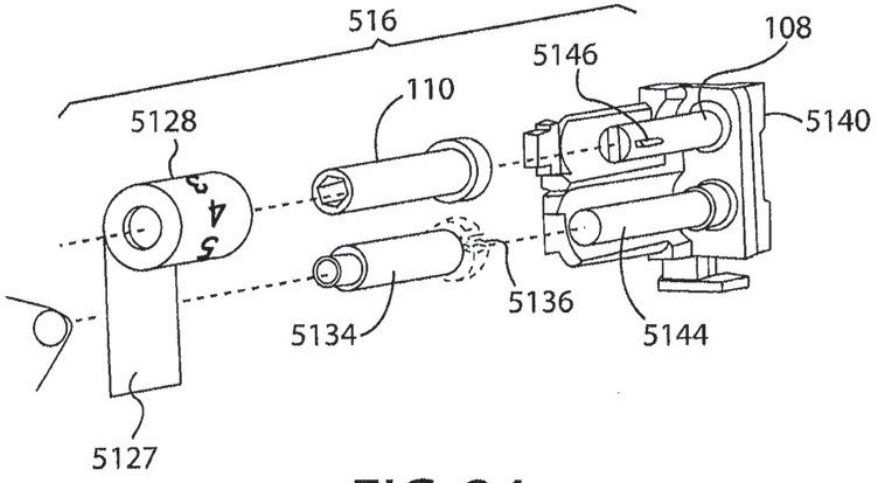

516
108
5146
110
5128
5140
5134
5136
5144
5127

FIG. 24

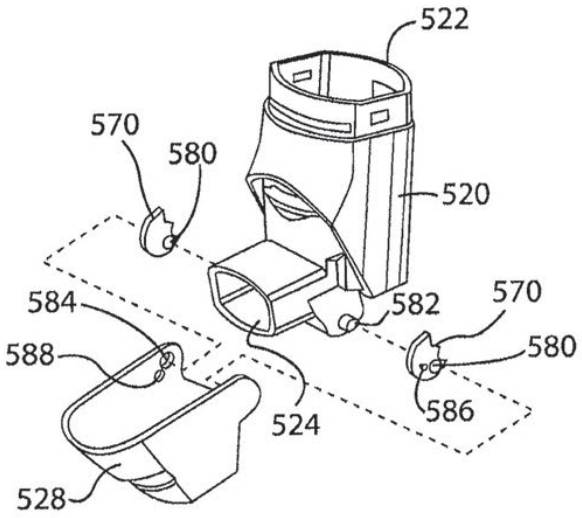


FIG. 25

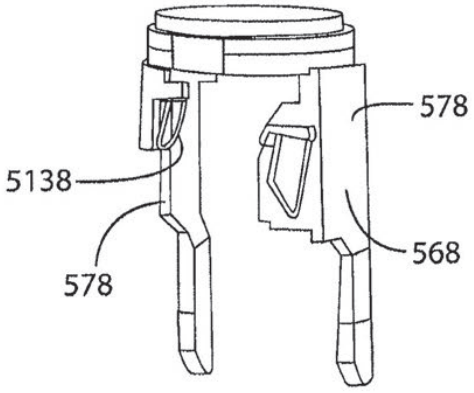


FIG. 26

DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation patent application of U.S. Non-Provisional patent application Ser. No. 14/103,324, filed Dec. 11, 2013, which is a divisional patent application of U.S. Non-Provisional patent application Ser. No. 13/110,532, filed May 18, 2011, now U.S. Pat. No. 8,978,966, issued Mar. 17, 2015, which claims priority to U.S. Provisional Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Provisional Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for any and all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-dawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30 N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler is closed. Due to the way in which the mouthpiece is opened and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/−0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections maybe provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is

arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an otherwise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf my also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is be highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is high advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter

display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia. The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. **1** is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. **2** is a top plan view of the components as shown in FIG. **1**;

FIG. **3**A is a section on the plane **3**A-**3**A in FIG. **2**;

FIG. **3**B is a view corresponding to FIG. **3**A but with a dose counter fitted to the main body of the inhaler;

FIG. **4**A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. **4**B is a view in the direction **4**B in FIG. **4**C of a spring retainer of the dose counter;

FIG. **4**C is a top view of the spring retainer of FIG. **4**B;

FIG. **5** is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. **6**A, **6**B, **6**C, **6**D, **6**E, **6**F, **6**G and **6**H are various views of dose counter components of the inhaler;

FIGS. **7**A and **7**B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. **7**C is a further sectional view similar to that of FIG. **7**B but with the canister removed;

FIG. **7**D is a top plan view of the inhaler main body;

FIGS. **8**A, **8**B, **8**C and **8**D show the inhaler main body and dose counter components during assembly thereof;

FIG. **9** shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. **10**A, **10**B, **10**C, **10**D, **10**E and **10**F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. **11** shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. **12** is an enlarged version of part of FIG. **4**A;

FIG. **13** shows an end portion of a tape of the dose counter;

FIG. **14** shows a computer system for designing the dose counter;

FIG. **15** is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. **1** to **14**;

FIG. **16** shows an end view of the stock bobbin of FIG. **15**;

FIG. **17** is a section through a longitudinal axis of the stock bobbin of FIGS. **15** and **16**;

FIGS. **18**A, **18**B and **18**C are views of the stock bobbin of FIGS. **15** to **17** mounted in the dose counter chassis of FIGS. **1** to **14**, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. **6**F, with the forks in a compressed configuration;

FIGS. **19**A, **19**B and **19**C are views equivalent to FIGS. **18**A to **18**C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. **20** is an isometric view of the chassis assembled and including the stock bobbin of FIGS. **15** to **17** but excluding the tape for reasons of clarity;

FIG. **21** is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. **22** is an exploded view of the inhaler of FIG. **21**;

FIG. **23** is a view of a dose counter of the inhaler of FIG. **21**;

FIG. **24** is an exploded view of the dose counter shown in FIG. **23**;

FIG. **25** is an exploded view of parts of the inhaler of FIG. **21**; and

FIG. **26** is a view of a yoke of the inhaler of FIG. **21**.

DETAILED DESCRIPTION OF THE INVENTION

FIG. **1** shows a main body **10** of a manually operated metered dose inhaler **12** in accordance with an embodiment related to the present invention and having a mouthpiece cap **14** securable over a mouthpiece **16** of the main body.

The main body has a canister chamber **18** into which a canister **20** (FIG. **7**A) is slideable. The canister **20** has a generally cylindrical main side wall **24**, joined by a tapered section **26** to a head portion **28** having a substantially flat lower face **30** which has an outer annular drive surface **32** arranged to engage upon and drive an actuation pin **34** of a dose counter **36** as will be described. Extending centrally and axially from the lower face **30** is a valve stem **38** which is arranged to sealingly engage in a valve stem block **40** of the main body **10** of the inhaler **12**. The valve stem block **40** has a passageway **42** leading to a nozzle **44** for directing the contents of the canister **20**, namely active drug and propellant, towards an air outlet **46** of the inhaler main body **12**. It will be appreciated that due to gaps **48** between the canister **20** and an inner wall **50** of the main body **10** of the inhaler **12** an open top **52** of the main body **10** forms an air inlet into the inhaler **12** communicating via air passageway **54** with the air outlet **46**, such that canister contents exiting nozzle **44** mix with air being sucked by the user through the air passageway **54** in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter **36** will now be described. The dose counter **36** includes an actuation pin **34** biased upwardly from underneath by a return spring **56** once installed in the main body **10**. As best shown in FIGS. **4**A, **6**H and **8**A, the pin **34** has side surfaces **58**, **60** arranged to slide between corresponding guide surfaces **62**, **64** located in a dose counter chamber **66** of the main body **10**, as well as an end stop surface **68** arranged to engage a corresponding end stop **70** formed in the dose counter chamber **66** to limit upward movement of the pin **34**. The pin **34** has a top part **72** which is circularly cylindrical and extends through an aperture **74** formed through a separator wall **76** which separates the canister chamber **18** from the dose counter chamber **66**. The top part **72** of the pin **34** has a flat top surface **78** which is arranged to engage the outer annular drive surface **32** of the canister **20**.

The actuation pin **34** is integrally formed with a drive or actuator pawl **80**. The actuator pawl **80** has a generally inverted U-shape configuration, having two mutually spaced and parallel arms **82**, **84** extending from a base portion of the actuation pin **34**, each holding at respective distal ends **88** thereof opposite ends of a pawl tooth member **90** which extends in a direction substantially perpendicular to the arms **82**, **84**, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth **92** of a ratchet wheel **94** of an incremental drive system **96** or ratchet mechanism **96** of the dose counter **36**. As shown for example in FIG. **10**B, the pawl tooth member **90** has a sharp lower

longitudinal side edge **98** arranged to engage the drive teeth **92**, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl **80** and resultant rotational positioning of the ratchet wheel **94**.

The dose counter **36** also has a chassis preassembly **100** which, as shown in FIGS. **4**A and **6**A, includes a chassis **102** having a first shaft **104** receiving the ratchet wheel **94** which is secured to a tape reel shaft **106**, and a second shaft (or split pin) **108** which is parallel to and spaced from the first shaft **104** and which slidably and rotationally receives a tape stock bobbin **110**.

As shown in FIG. **6**B, when the inhaler has not been used at all, the majority of a tape **112** is wound on the tape stock bobbin **110** and the tape **112** has a series of regularly spaced numbers **114** displayed therealong to indicate a number of remaining doses in the canister **20**. As the inhaler is repeatedly used, the ratchet wheel **94** is rotated by the actuator pawl **80** due to operation of the actuation pin **34** by the canister **20** and the tape **112** is incrementally and gradually wound on to the tape reel shaft **106** from the second shaft **108**. The tape **112** passes around a tape guide **116** of the chassis **102** enabling the numbers **114** to be displayed via a window **118** in a dose counter chamber cover **120** having a dose marker **132** formed or otherwise located thereon.

As shown in FIGS. **6**A and **6**D, the second shaft **108** is forked with two forks **124**, **126**. The forks **124**, **126** are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft **108** friction or control elements **128**, **130**, one on each fork. Each control element extends longitudinally along its respective fork **124**, **126** and has a longitudinally extending friction surface **132**, **134** which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore **136** inside the tape stock bobbin **110**. This control arrangement provided between the bore **136** and the control elements **128**, **130** provides good rotational control for the tape stock bobbin **110** such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin **110** and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. **6**D, as well as FIGS. **6**G and **10**A to **10**F, the chassis **102** is provided with an anti-back drive tooth **138** or count pawl **138** which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. **10**A to **10**F, when the actuation pin **34** is depressed fully so as to fire the metered valve (not shown) inside the canister **20**, the actuator pawl **80** pulls down on one of the teeth **92** of the ratchet wheel **94** and rotates the wheel **94** anticlockwise as shown in FIG. **6**D so as to jump one tooth **92** past the count pawl **138**, thereby winding the tape **112** a distance incrementally relative to the dose marker **122** on the dose counter chamber **120** so as to indicate that one dose has been used.

With reference to FIG. **10**B, the teeth of the ratchet wheel **94** have tips **143** which are radiused with a 0.1 mm radius between the flat surfaces **140**, **142**. The ratchet wheel **94** has a central axis **145** which is 0.11 mm above datum plane **220** (FIG. **9**). A top/nose surface **147** of the anti-back drive tooth **138** is located 0.36 mm above the datum plane **220**. The distance vertically (i.e. transverse to datum plane **220**—FIG. **9**) between the top nose surface **147** of the anti-back drive tooth is 0.25 mm from the central axis **145** of the wheel **94**. Bump surface **144** has a lateral extent of 0.20 mm, with a vertical length of a flat **145'** thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis **145**), the top **149** of the bump surface **144** being 3.02 mm vertically below the axis **145**, and the flat **145'** being spaced a distance sideways (i.e. parallel to the datum plane **220**) 2.48 mm from the axis **145**. The top surface **78** of the pin **34** (FIG. **6**H) is 11.20 mm above the datum plane **220** (FIG. **9**) when the actuator pawl **80** and pin **34** are in the start configuration. The length of the valve stem **22** is 11.39 mm and the drive surface **32** of the canister **20** is 11.39 mm above the datum plane **220** when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister **20** and the pin **34** in this configuration.

FIGS. **10**A and **10**B show the actuator pawl **80** and ratchet wheel **94** and count pawl **138** in a start position in which the flat top **78** of the pin **34** has not yet been engaged by the outer annular drive surface **32** of the canister **20** or at least has not been pushed down during a canister depression.

In this "start" position, the count pawl **138** engages on a non-return back surface **140** of one of the teeth **92** of the ratchet wheel **94**. The lower side edge **98** of the actuator pawl is a distance "D" (FIG. **9**) 1.33 mm above datum plane **220** which passes through bottom surface or shoulder **41** of valve stem block **40**, the datum plane **220** being perpendicular to a main axis "X" of the main body **10** of the inhaler **12** which is coaxial with the centre of the valve stem block bore **43** and parallel to a direction of sliding of the canister **20** in the main body **10** of the inhaler **12** when the canister is fired.

As shown in FIG. **10**B, an advantageous feature of the construction is that the pawl tooth/actuator **90** acts as a supplementary anti-back drive member when the inhaler **12** is not being used for inhalation. In particular, if the inhaler **12** is accidentally dropped, resulting in a jolt to the dose counter **36** then, if the wheel **94** would try to rotate clockwise (backwards) as shown in FIG. **10**B, the back surface **140** of a tooth will engage and be blocked by the tooth member **90** of the pawl **80**. Therefore, even if the anti-back drive tooth **138** is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel **94** is prevented and, upon the next canister firing sequence, the pawl **90** will force the wheel **94** to catch up to its correct position so that the dose counter **36** continues to provide correct dosage indication.

FIG. **10**C shows a configuration in which the actuator pawl **80** has been depressed with the pin **34** by the canister **20** to a position in which the side edge **98** of the pawl tooth member **90** is just engaged with one of the teeth **92** and will therefore upon any further depression of the pin **34** begin to rotate the wheel **94**. This is referred to as a "Reset" position or configuration. In this configuration, the lower side edge **98** of the actuator **80** is 0.64 mm above the datum plane **220**.

FIG. **10**D shows a configuration in which the actuator pawl **80** has been moved to a position lower than that shown in FIG. **10**C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle **44**. It will be noted that in this configuration the count pawl **138** is very slightly spaced from the back surface **140** of the same tooth **92** that it was engaging in the configuration of FIG. **10**D. The configuration shown in FIG. **10**D is known as a "Fire" configuration. In this configuration the lower side edge **98** of the actuator **80** is 0.47 mm below the datum plane **220**.

FIG. **10**E shows a further step in the sequence, called a "Count" position in which the actuator pawl **80** has rotated the ratchet wheel **94** by the distance circumferentially angularly between two of the teeth **92**, such that the count pawl **138** has just finished riding along a forward surface **142** of one of the teeth **92** and has resiliently jumped over the tooth

into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10**F, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6**G) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10**F will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10**F.

As shown in FIGS. **7**C and **7**D, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7**B a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7**A and schematically in FIG. **7**B, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** a as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **144**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7**C for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8**A, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8**B, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4**B, **4**C and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6**B) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6**B may as shown in FIG. **8**C be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8**D, the

dose counter chamber **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8**D being "200", thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8**D, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18**C and **19**C, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6**F. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radio extent of the control elements **128**, **130**, is 3.1 millimeters and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18**C and **19**C is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18**A to **18**C when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19**A to **19**C, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**

It will be appreciated that whereas FIGS. **18**B and **19**B are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18**A and **19**A are cross-sections. FIG. **19**A is a section on the plane A-A' in FIG. **19**C and FIG. **18**A is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

As the inhaler **12** is used and the ratchet wheel **94** rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin **108** at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin **108** at such rotational positions and this may involve a click forward of the stock bobbin **110** to the next position equivalent to that in FIGS. **19**A to **19**C in which the control elements **128**, **130** of the split pin art located in the concavities **302**. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape **112** from loosening during transit if the inhaler **12** is dropped, such as onto a hard surface. This is highly advantageous, since the tape **11** is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. **18**C and **19**C, the forks **124**, **126** rotate about a point **316** on the split pin where the forks **124**, **126** come together. This rotational action means that there is a camming action between the forks **124**, **126** and the engagement surface **300** without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface **300** and forks **124**, **126** are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler **12** is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape **112** to overcome the regulator at the stock bobbin **110**. 0.32 N is achieved with the control elements **128** having the profile shown in FIG. **19**C and 0.38 N is achieved with the profile of the control elements **128** altered to be as shown as described with reference to FIG. **6**F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. **15** to **20** does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape **112** as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape **112** can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities **302** and convex wall portions **304**, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements **128**, **130** are provided, so that all of the control elements **128**, **130** will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface **300** on the inside of the stock bobbin **110**, it could be placed on the outside of the stock bobbin **110** so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface **300** and forks **124**, **126** does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel **94**. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin **110** can be wound backwards during or after fitting the bobbin **100**, shaft **106** and tape **112** onto the carriage **102**, if desired.

The stock bobbin **110** and the carriage **102** including the split pin **108** are both moulded of polypropylene material.

It will be seen from FIG. **16** that the cross-sectional shape **301** is not symmetrical within the hexagonal socket **204**. This has enabled the hexagonal socket **204** to be maintained at a useful size while still allowing the desired size and geometry of the cross section **301** to fit without interfering with the hexagonal shape of the hexagonal socket **204** and also permits moulding to work during manufacture.

As shown in FIG. **17**, the stock bobbin **110** has a series of four circumferential ribs **330** inside it and a spaced thereabout. These hold the stock bobbin **110** on the correct side of the mould tool during moulding.

FIGS. **21** and **22** show a preferred embodiment in accordance with the invention of an inhaler **510** for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler **510** is as disclosed in FIGS. **1** to **16** or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin **110** and second shaft **108** of the dose counter **516** modified so as to be as in FIGS. **15** to **20** hereof. Thus, the dry powder inhaler **510** generally includes a housing **518**, and an assembly **512** received in the housing (see FIG. **21**). The housing **518** includes a case **520** having an open end **522** and a mouthpiece **524** (FIG. **25**) for patient inhalation, a cap **526** secured to and closing the open end **522** of the case **520**, and a cover **528** pivotally mounted to the case **520** for covering the mouthpiece **524**. As shown in FIG. **22**, the inhaler **510** also includes an actuation spring **569**, first yoke **566** with opening **572**, bellows **540** with crown **574**, a reservoir **514**, second yoke **568** with hopper **542** and dose counter **516** mounted thereto, and case **520** has transparent window **5130** thereon for viewing dose counter tape indicia **5128**. The dose metering system also includes two cams **570** mounted on the mouthpiece cover **528** and movable with the cover **528** between open and closed positions. The cams **570** each include an opening **580** for allowing outwardly extending hinges **582** of the case **520** to pass therethrough and be received in first recesses **584** of the cover **528**. The cams **570** also include bosses **586** extending outwardly and received in second recesses **588** of the cover **528**, such that the cover **528** pivots about the hinges **582** and the cams **570** move with the cover **528** about the hinges **582**. As described in EP-A-1330280, cams **570** act upon cam followers **578** to move second yoke **568** up and down and thereby operate dose counter by engagement of pawl **5138** on the second yoke **568** with teeth **5136**. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system **516** therefore includes a ribbon or tape **5128** (FIGS. **23** & **24**), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window **5130** provided in the housing **18** (see FIG. **22**). The dose counting system **516** includes the rotatable stock bobbin **110** (as described above), an indexing spool **5134** rotatable in a single direction, and the ribbon **5128** rolled and received on the bobbin **110** and having a first end **5127** secured to the spool **5134**, wherein the ribbon **5128** unrolls from the bobbin **110** so that the indicia are successively displayed as the spool **5134** is rotated or advanced. In FIGS. **23** and **24** the wavelike engagement surface **300** of the bobbin **110** is not shown for the purposes of clarity.

The spool **134** is arranged to rotate upon movement of the yokes **566**, **568** to effect delivery of a dose of medicament from reservoir **514**, such that the number on the ribbon **5128** is advanced to indicate that another dose has been dispensed by the inhaler **510**. The ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase or

decrease upon rotation of the spool **5134**. For example, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool **5134** to indicate the number of doses remaining in the inhaler **510**. Alternatively, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool **5134** to indicate the number of doses dispensed by the inhaler **10**.

The indexing spool **5134** includes radially extending teeth **5136**, which are engaged by pawl **5138** extending from a cam follower **578** of the second yoke **568** upon movement of the yoke to rotate, or advance, the indexing spool **5134**. More particularly, the pawl **5138** is shaped and arranged such that it engages the teeth **5136** and advances the indexing spool **5134** only upon the mouthpiece cover **528** being closed and the yokes **566**, **568** moved back towards the cap **526** of the housing **518**.

The dose counting system **516** also includes a chassis **5140** that secures the dose counting system to the hopper **542** and includes shafts **108**, **5144** for receiving the bobbin **110** and the indexing spool **5134**. As described above with reference to FIGS. **1** to **20**, the bobbin shaft **108** is forked and includes radially nubs **5146** for creating a resilient resistance to rotation of the bobbin **110** on the shaft **108** by engaging with the wavelike engagement surface **300** inside the bobbin **110**. A clutch spring **5148** is received on the end of the indexing spool **5134** and locked to the chassis **5140** to allow rotation of the spool **5134** in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed is:

1. An inhaler for metered dose inhalation, the inhaler comprising:

a main body having a canister housing,

a medicament canister, which is moveable relative to the canister housing and retained in a central outlet port of the canister housing arranged to mate with a canister fire stem of the medicament canister, and

a dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of the medicament canister,

wherein the canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall,

wherein the canister housing has a longitudinal axis X which passes through the center of the central outlet port, and

wherein the first inner wall canister support formation, the actuation member, and the central outlet port lie in a common plane coincident with the longitudinal axis X such that the first inner wall canister support formation protects against unwanted actuation of the dose counter by reducing rocking of the medicament canister relative to the main body of the inhaler.

2. The inhaler as claimed in claim **1** wherein the medicament canister is movable relative to the dose counter.

3. The inhaler as claimed in claim **1** further comprising an aperture formed in the inner wall through which the portion of the actuation member extends.

4. The inhaler as claimed in claim **1**, wherein the first inner wall canister support formation comprises a support rail which extends longitudinally along an inside surface of the main body.

5. The inhaler as claimed in claim **4**, wherein the support rail includes a step formed thereon.

6. The inhaler as claimed in claim **4** further comprising a plurality of support rails each of which extends longitudinally along the inside surface of the main body.

7. The inhaler as claimed in claim **6**, wherein two of the plurality of support rails are positioned at opposite ends of the inside surface of the main body to face each other.

8. The inhaler as claimed in claim **4**, wherein the support rail includes two steps formed thereon, the steps being spaced apart longitudinally along an inside surface of the main body.

9. The inhaler as claimed in claim **4**, wherein the support rail merges with the inner wall at a location adjacent the aperture.

10. The inhaler as claimed in claim **9**, wherein a width dimension of the support rail is not constant, and the width dimension is greatest at the location where the support rail merges with the inner wall.

11. The inhaler as claimed in claim **1** further comprising a second inner wall canister support formation and wherein the second inner wall canister support formation, the first inner wall canister support formation, the actuation member and the central outlet port lie in a common plane coincident with longitudinal axis X.

12. An inhaler for metered dose inhalation, the inhaler comprising:

a main body having a canister housing,

a medicament canister, which is moveable relative to the canister housing and retained in a central outlet port of the canister housing arranged to mate with a canister fire stem of the medicament canister, and

a dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of the medicament canister,

wherein the canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall,

wherein the canister housing has a longitudinal axis X which passes through the center of the central outlet port, and

wherein the first inner wall canister support formation, the actuation member, and the central outlet port lie in a common plane coincident with the longitudinal axis X such that the first inner wall canister support formation protects against dose count errors by reducing rocking of the medicament canister towards or away from the actuation member.

13. An inhaler for metered dose inhalation, the inhaler comprising:

a main body having a canister housing,

a medicament canister retained in the canister housing and movable relative thereto, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of the medicament canister,

wherein the canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall,

wherein the canister housing has an aperture formed in the inner wall through which the portion of the actuation member extends, and

wherein the first inner wall canister support formation extends from the main surface of the inner wall to the aperture.

14. The inhaler as claimed in claim **13** wherein the medicament canister is movable relative to the dose counter.

15. The inhaler as claimed in claim **13**, wherein the first inner wall canister support formation comprises a support rail which extends longitudinally along an inside surface of the main body.

16. The inhaler as claimed in claim **15**, wherein the support rail includes a step formed thereon.

17. The inhaler as claimed in claim **15** further comprising a plurality of support rails each of which extends longitudinally along the inside surface of the main body.

18. The inhaler as claimed in claim **17**, wherein two of the plurality of support rails are positioned at opposite ends of the inside surface of the main body to face each other.

19. The inhaler as claimed in claim **15**, wherein the support rail includes two steps formed thereon, the steps being spaced apart longitudinally along the inside surface of the main body.

20. The inhaler as claimed in claim **15**, wherein a width dimension of the support rail is not constant, and the width dimension is greatest at the location where the support rail is closest to the aperture.

21. The inhaler as claimed in claim **13**, wherein the first inner wall canister support formation, the aperture, and a central outlet port of the canister housing arranged to mate with a canister fire stem of the medicament canister, all lie in a common plane coincident with a longitudinal axis X which passes through the center of the central outlet port.

22. The inhaler as claimed in claim **21** further comprising a second inner wall canister support formation and wherein the second inner wall canister support formation, the first inner wall canister support formation, the aperture, and the central outlet port lie in a common plane coincident with longitudinal axis X.

* * * * *

Exhibit D

US010561808B2

(12) **United States Patent**
Walsh et al.

(10) **Patent No.: US 10,561,808 B2**
(45) **Date of Patent: Feb. 18, 2020**

(54) **DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR**

(71) Applicants: **IVAX PHARMACEUTICALS IRELAND**, Waterford (IE); **NORTON (WATERFORD) LIMITED**, Waterford (IE); **TEVA PHARMACEUTICALS IRELAND**, Waterford (IE)

(72) Inventors: **Declan Walsh**, County Kilkenny (IE); **Derek Fenlon**, County Wexford (IE); **Simon Kaar**, County Cork (IE); **Jan Geert Hazenberg**, County Kilkenny (IE); **Daniel Buck**, County Waterford (IE); **Paul Clancy**, Waterford (IE); **Robert Charles Uschold**, Leominster, MA (US); **Jeffrey A. Karg**, Hopkinton, MA (US)

(73) Assignees: **IVAX PHARMACEUTICALS IRELAND**, Waterford (IE); **NORTON (WATERFORD) LIMITED**, Waterford (IE); **TEVA PHARMACEUTICALS IRELAND**, Waterford (IE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 228 days.

(21) Appl. No.: **15/262,818**

(22) Filed: **Sep. 12, 2016**

(65) **Prior Publication Data**

US 2016/0375208 A1 Dec. 29, 2016

Related U.S. Application Data

(60) Continuation of application No. 14/699,584, filed on Apr. 29, 2015, which is a continuation of application (Continued)

(51) **Int. Cl.**
A61M 15/00 (2006.01)
G06M 1/24 (2006.01)
A61M 11/00 (2006.01)

(52) **U.S. Cl.**
CPC ..... ***A61M 15/0078*** (2014.02); ***A61M 11/00*** (2013.01); ***A61M 15/007*** (2014.02); (Continued)

(58) **Field of Classification Search**
CPC ..... A61M 15/0078; A61M 15/0025; A61M 15/0026; A61M 15/007; A61M 15/0071; (Continued)

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,174,890 A 11/1979 Johnson
4,669,838 A 6/1987 Hibbard
(Continued)

FOREIGN PATENT DOCUMENTS

CA 2501726 9/2006
EP 1330280 7/2003
(Continued)

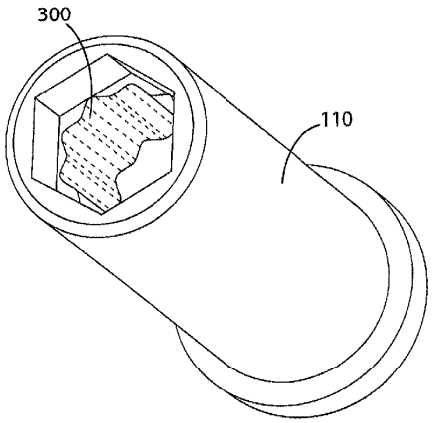
OTHER PUBLICATIONS

Final Office Action dated Oct. 20, 2016 for U.S. Appl. No. 14/699,567.
(Continued)

Primary Examiner — Daniel A Hess
(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP

(57) **ABSTRACT**

A dose counter for an inhaler includes a counter display arranged to indicate dosage information, and a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input. A regulator is provided which is arranged (Continued)



to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

29 Claims, 17 Drawing Sheets

Related U.S. Application Data

No. 14/103,353, filed on Dec. 11, 2013, now Pat. No. 9,526,850, which is a division of application No. 13/110,532, filed on May 8, 2011, now Pat. No. 8,978,966.

(60) Provisional application No. 61/345,763, filed on May 18, 2010, provisional application No. 61/417,659, filed on Nov. 29, 2010.

(52) **U.S. Cl.**
CPC ***A61M 15/009*** (2013.01); ***A61M 15/0025*** (2014.02); ***A61M 15/0026*** (2014.02); ***A61M 15/0065*** (2013.01); ***A61M 15/0071*** (2014.02); ***G06M 1/246*** (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)

(58) **Field of Classification Search**
CPC A61M 11/00; A61M 15/0065; A61M 15/009; G06M 1/246
USPC 235/8
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,687,359	A	8/1987	Barrus	
5,482,030	A	1/1996	Klein	
5,861,911	A	1/1999	Oosaka	
6,446,627	B1	9/2002	Bowman	
6,718,972	B2	4/2004	OLeary	
8,418,690	B2	4/2013	Power	
8,474,448	B2	7/2013	Oi	
8,978,966	B2	3/2015	Walsh et al.	
9,174,013	B2	11/2015	Walsh et al.	
9,463,289	B2	10/2016	Walsh et al.	
2002/0047021	A1	4/2002	Blacker	
2002/0078949	A1	6/2002	OLeary	
2002/0078950	A1*	6/2002	O'Leary	A61M 15/0045 128/200.22
2002/0084891	A1	7/2002	Mankins et al.	
2003/0209239	A1	11/2003	Rand	
2004/0089298	A1	5/2004	Haikarainen et al.	
2004/0095746	A1	5/2004	Murphy	
2005/0028815	A1	2/2005	Deaton	
2005/0087191	A1	4/2005	Morton	
2006/0096594	A1	5/2006	Bonney	
2006/0107949	A1	5/2006	Davies	
2006/0107979	A1	5/2006	Kim	
2007/0062518	A1	3/2007	Geser	
2008/0242465	A1	10/2008	Strobel	
2009/0178678	A1	7/2009	OLeary	
2010/0089395	A1	4/2010	Power	
2010/0218759	A1	9/2010	Anderson	
2011/0041845	A1	2/2011	Solomon	
2012/0006322	A1	1/2012	Anderson	

FOREIGN PATENT DOCUMENTS

EP	1486227	12/2004
GB	2320489	6/1998
JP	02502129	7/1990
JP	450059	8/1992
JP	07100205	4/1995
JP	10504220	4/1998
JP	2002528144	9/2002
JP	2004501685	1/2004
JP	2008-94103 A	4/2008
JP	2008094103	4/2008
JP	2008261423	10/2008
JP	2009233308	10/2009
JP	2009257392	11/2009
JP	2010096308	4/2010
WO	8909078	10/1989
WO	9628205	9/1996
WO	9828033	7/1998
WO	9936115	7/1999
WO	02/00281 A2	1/2002
WO	03101514	12/2003
WO	2005102430	11/2005
WO	2006062449	6/2006
WO	2006062449 A1	6/2006
WO	2007012861	2/2007
WO	2007062518	6/2007
WO	2008023019	2/2008
WO	2008119552	2/2008
WO	2011012325	2/2011
WO	2011012327	2/2011

OTHER PUBLICATIONS

Advisory Action dated Mar. 13, 2017 for U.S. Appl. No. 14/699,567.
Non-Final Office Action dated Jan. 12, 2017 for U.S. Appl. No. 14/713,620, 8 pages.
Final Rejection dated Sep. 27, 2016 for U.S. Appl. No. 14/699,578.
Final Office Action dated Aug. 31, 2016 for U.S. Appl. No. 14/713,620, 7 pages.
Advisory action dated Feb. 9, 2017 for U.S. Appl. No. 14/699,584.
Non-final rejection dated Jul. 12, 2016 for U.S. Appl. No. 14/713,643.
File History for U.S. Appl. No. 15/271,738.
File History for U.S. Appl. No. 15/269,102.
File History for U.S. Appl. No. 15/262,818.
File History for U.S. Appl. No. 15/289,553.
File History for U.S. Appl. No. 15/269,249.
Final rejection dated Oct. 20, 2016 or U.S. Appl. No. 14/699,584.
Non-Final Office Action dated Jun. 24, 2016 for U.S. Appl. No. 14/713,620, 7 pages.
Final rejection dated Oct. 20, 2016 or U.S. Appl. No. 14/713,631.
Advisory Action dated Mar. 16, 2017 or U.S. Appl. No. 14/713,633.
Entire patent prosecution history of U.S. Appl. No. 13/110,532, filed May 18, 2011, entitled,"Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,324, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,343, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,353, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,363, filed Dec. 1, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/103,392, filed Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/699,567, filed Apr. 29, 2015, entitled, "Dose Counter for Inhaler and Method for Counting Doses."
Entire patent prosecution history of U.S. Appl. No. 14/699,578, filed Apr. 29, 2015, entitled, "Dose Counter for Inhaler Having a Bore and Shaft Arrangement."
Entire patent prosecution history of U.S. Appl. No. 14/699,584, filed Apr. 29, 2015, entitled, "Dose Counter for Inhaler Having an Antireverse Rotation Actuator".

(56) **References Cited**

OTHER PUBLICATIONS

Entire patent prosecution history of U.S. Appl. No. 14/713,612, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/713,620, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
Entire patent prosecution history of U.S. Appl. No. 14/713,643, filed May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof."
European Patent Office Communication, dated Apr. 24, 2014 of counterpart European Patent Application No. 11 010 211.8.
European Patent Office Communication, dated Apr. 24, 2014 of counterpart European Patent Application No. 11 010 212.6.
First Examination Report of counterpart New Zealand Patent Application No. 603466, dated Jul. 1, 2013.

* cited by examiner

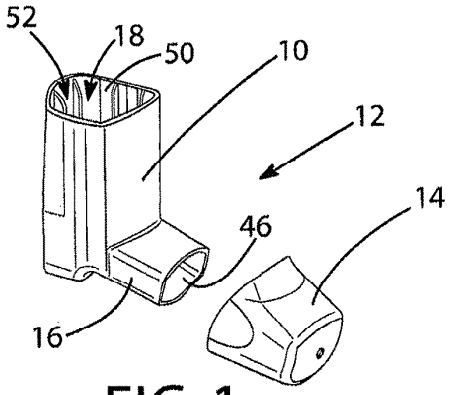


FIG. 1

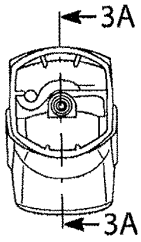


FIG. 2

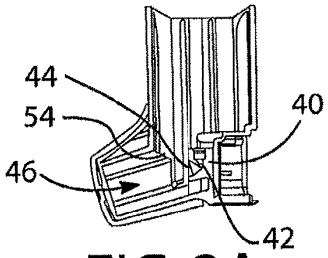


FIG. 3A

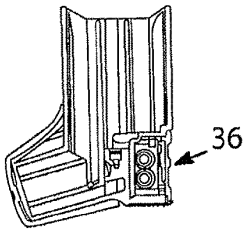


FIG. 3B

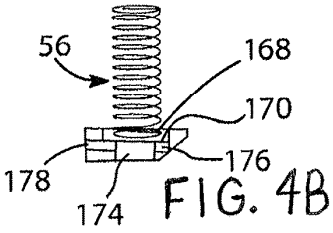


FIG. 4B

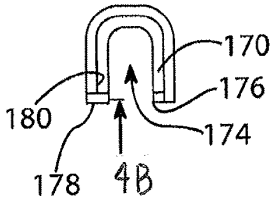


FIG. 4C

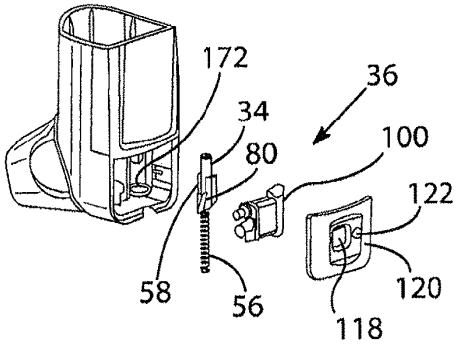


FIG. 4A

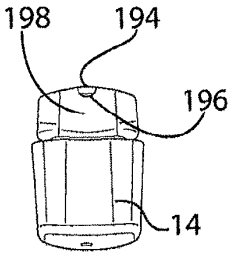


FIG. 5

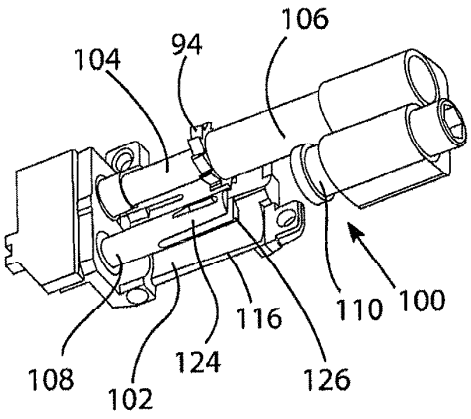


FIG. 6A

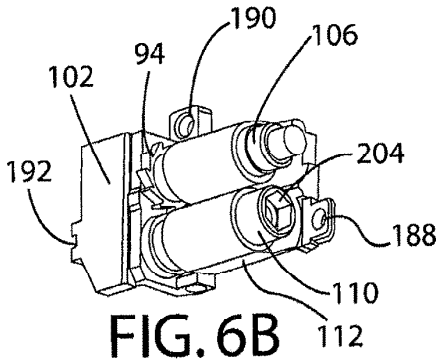


FIG. 6B

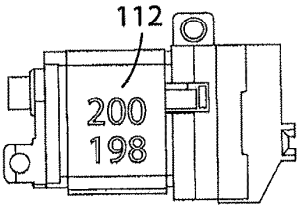


FIG. 6C

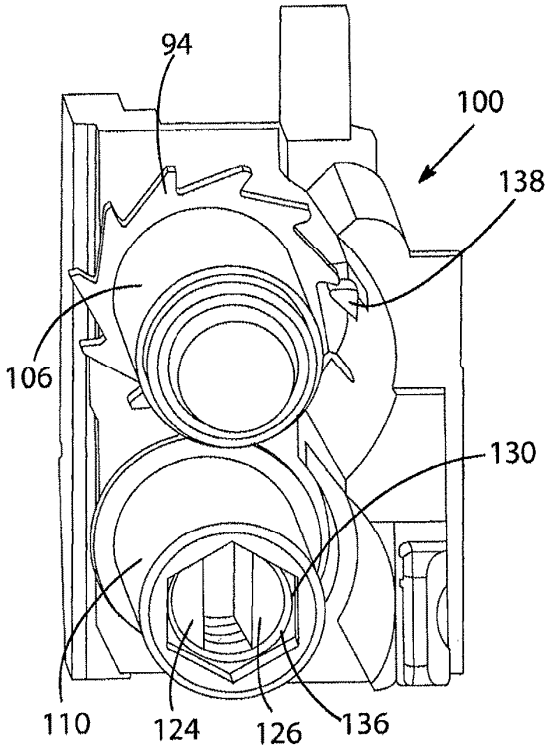


FIG. 6D

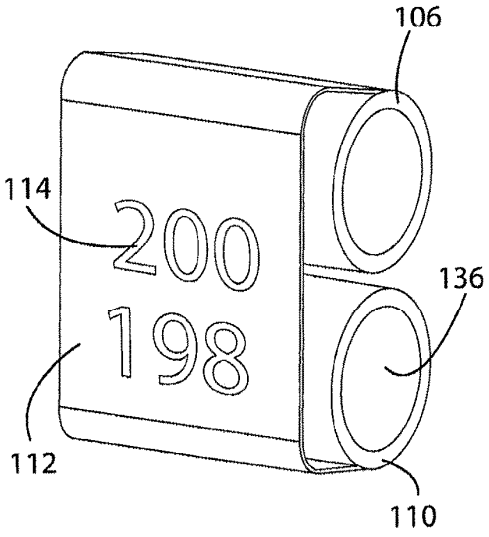


FIG. 6E

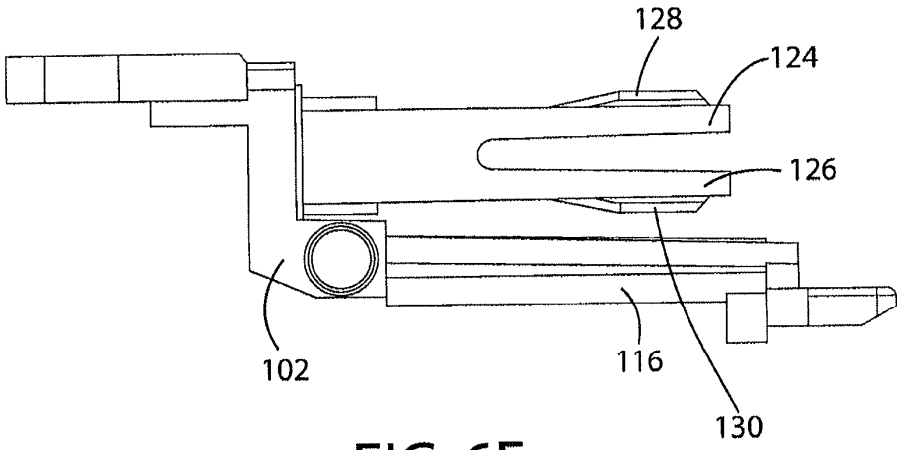


FIG. 6F

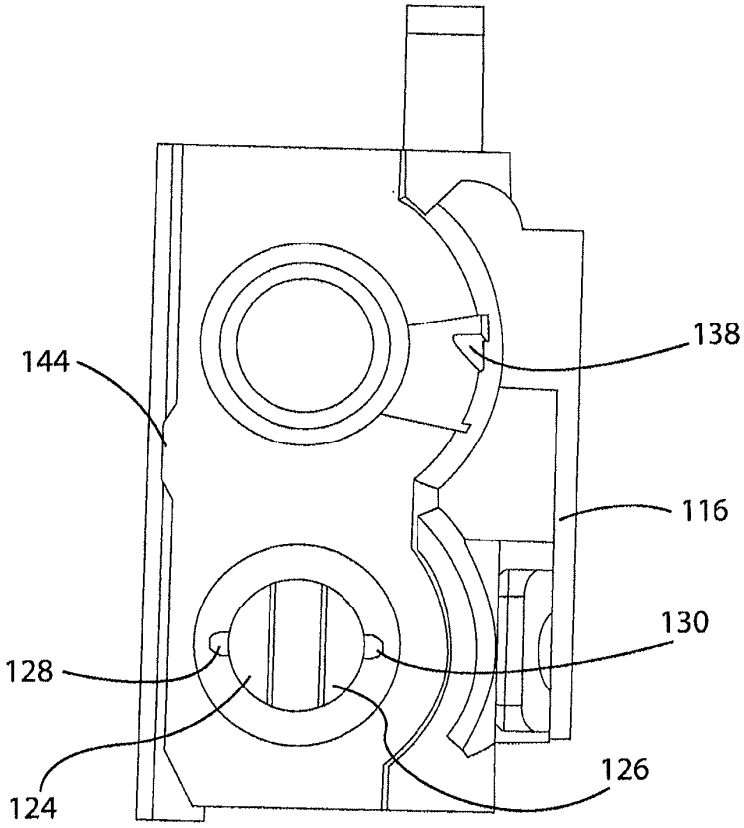


FIG. 6G

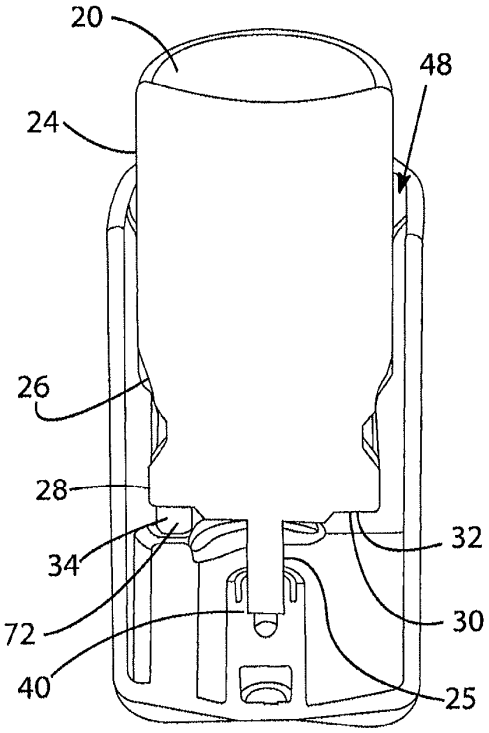


FIG. 7A

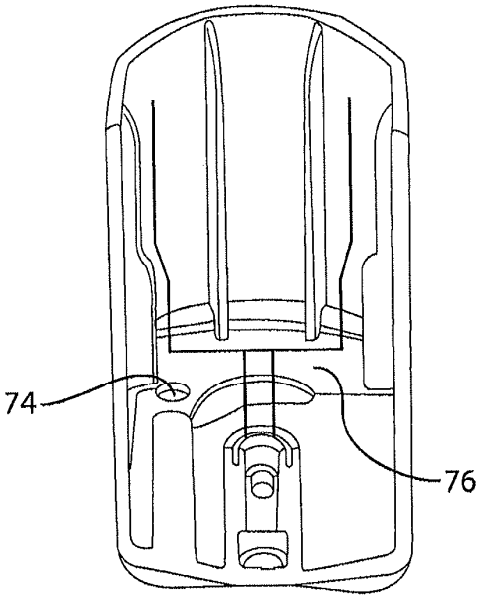


FIG. 7B

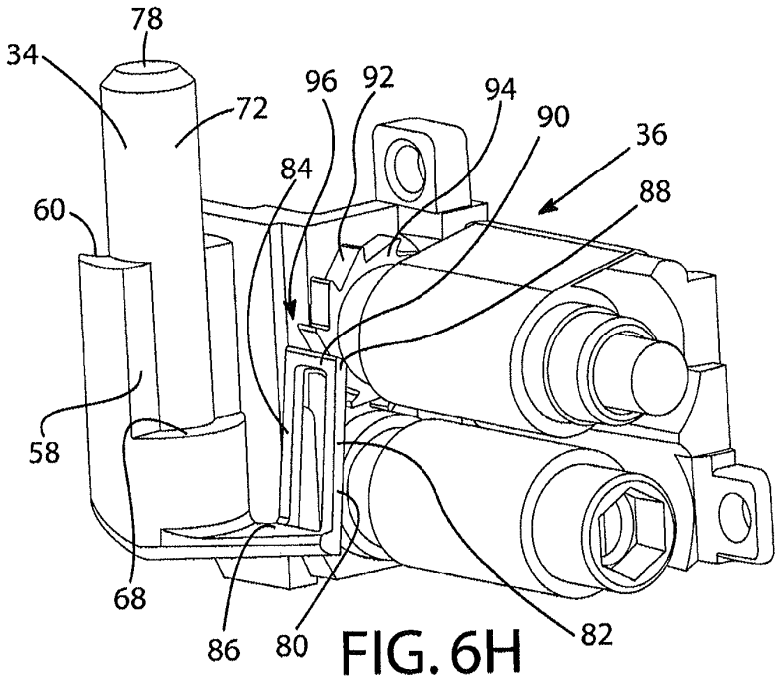


FIG. 6H

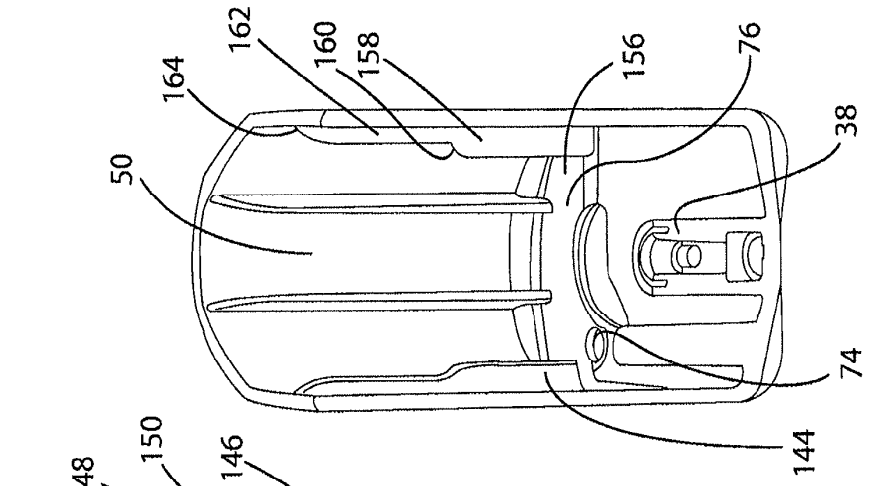


FIG. 7C

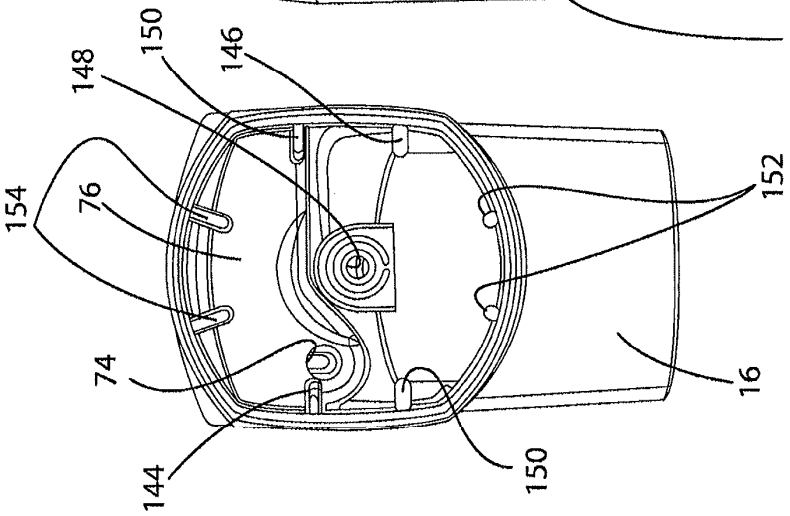


FIG. 7D

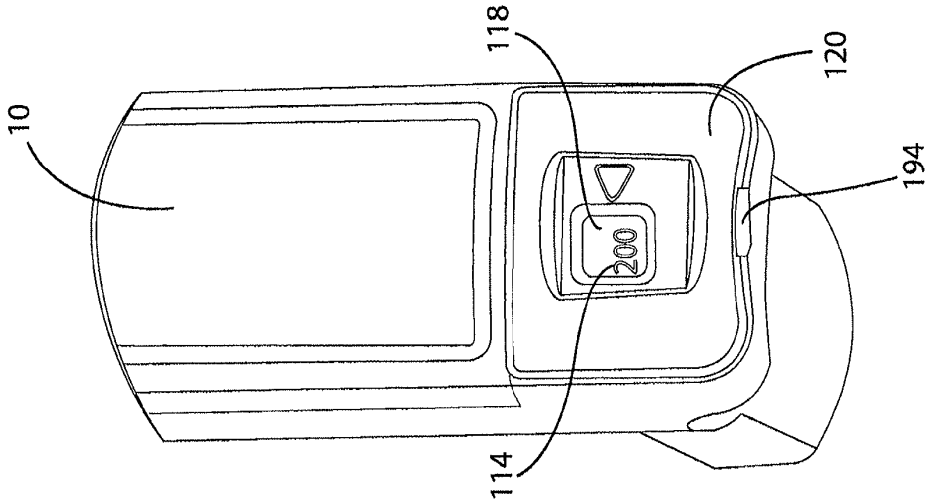


FIG. 8D

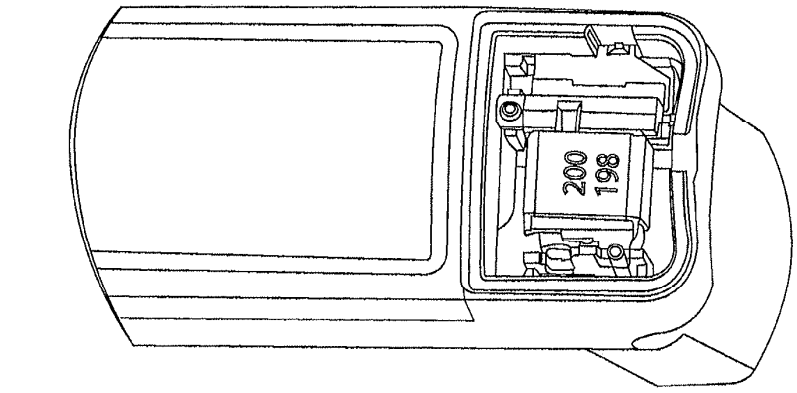


FIG. 8C

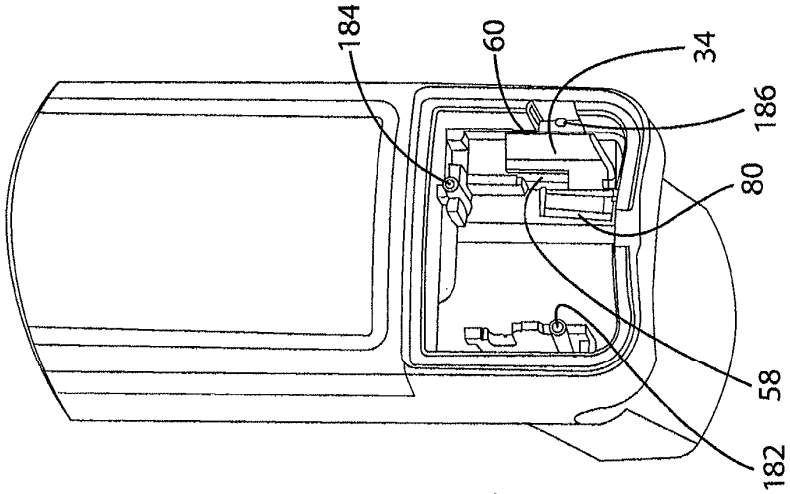


FIG. 8B

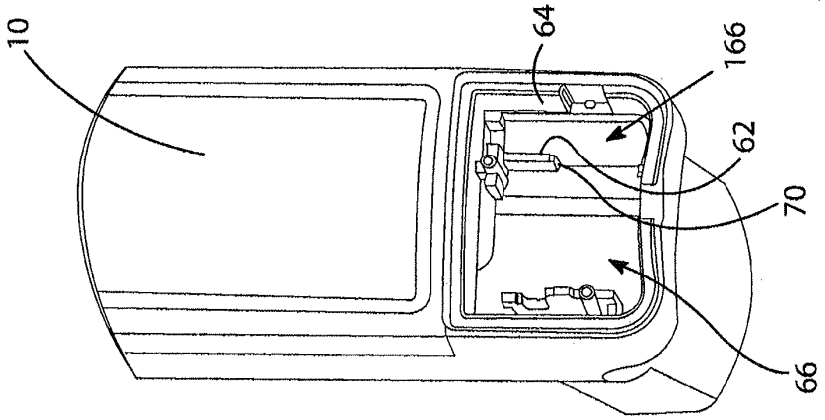


FIG. 8A

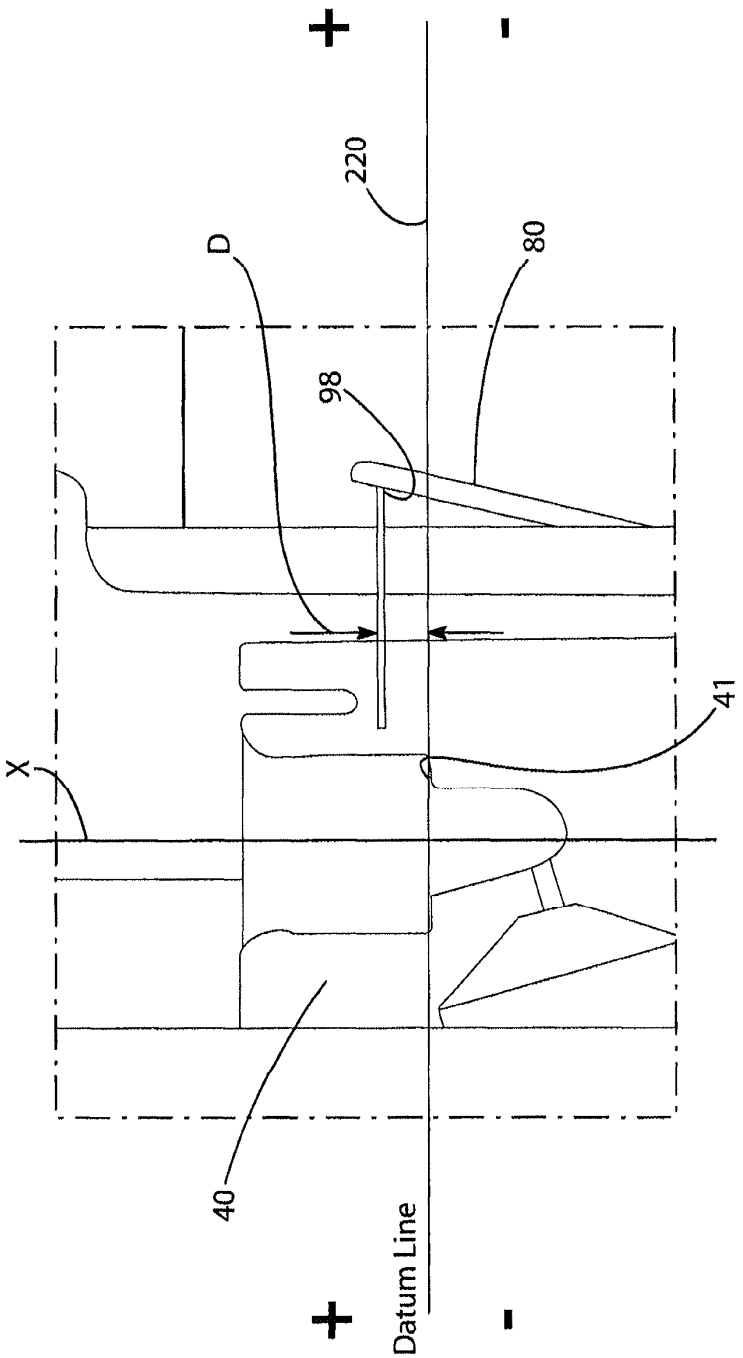


FIG. 9

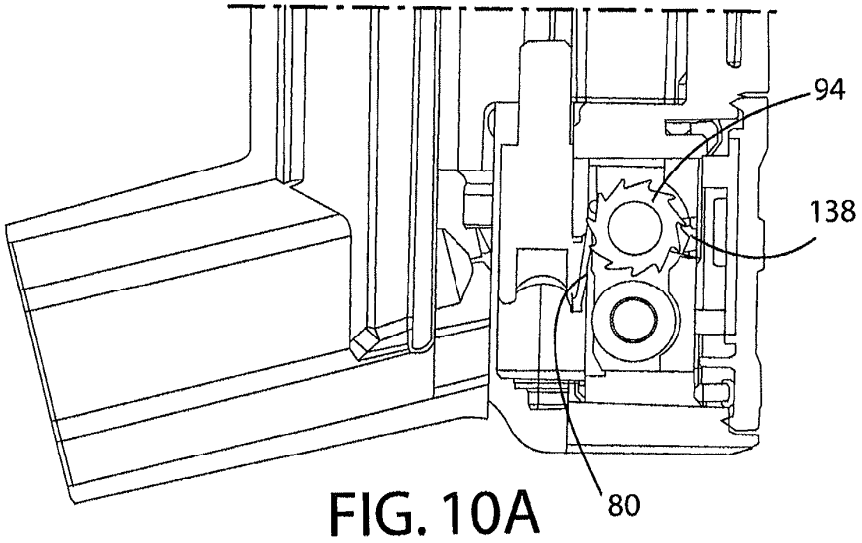


FIG. 10A

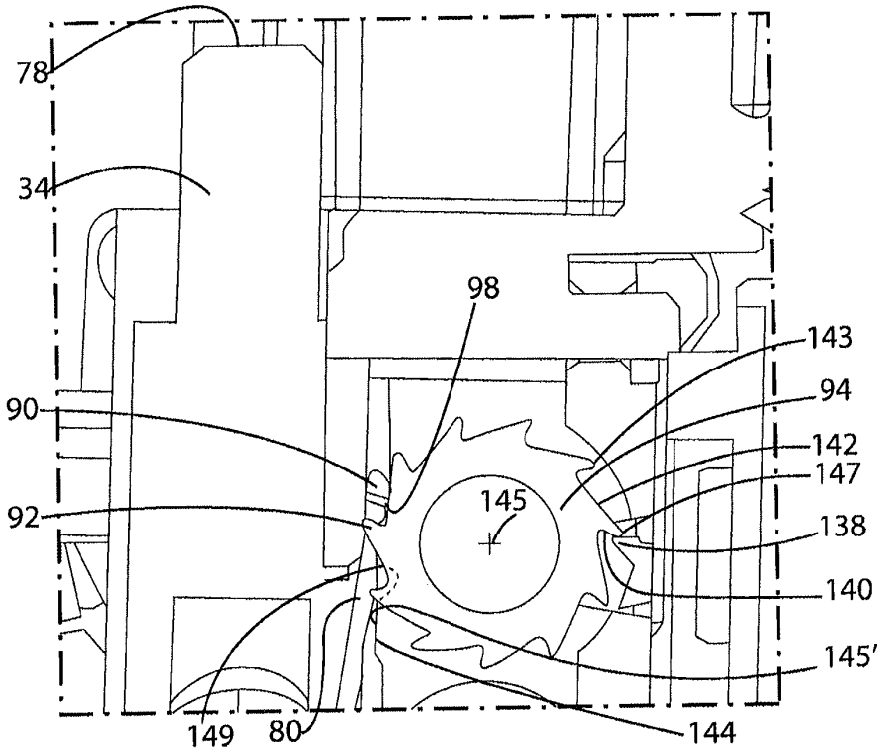


FIG. 10B

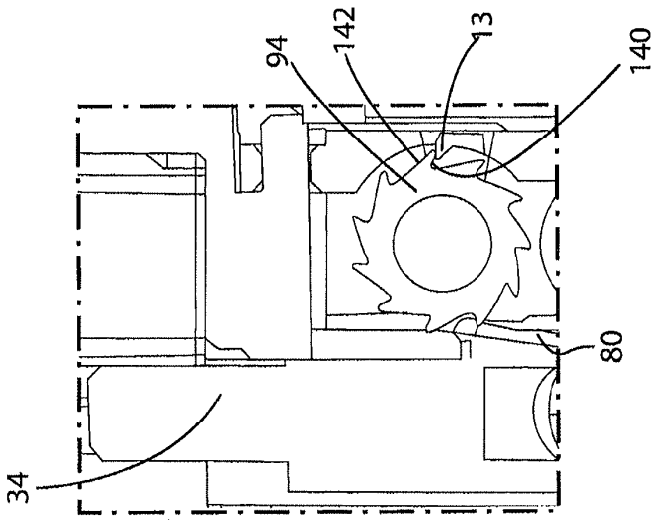


FIG. 10E

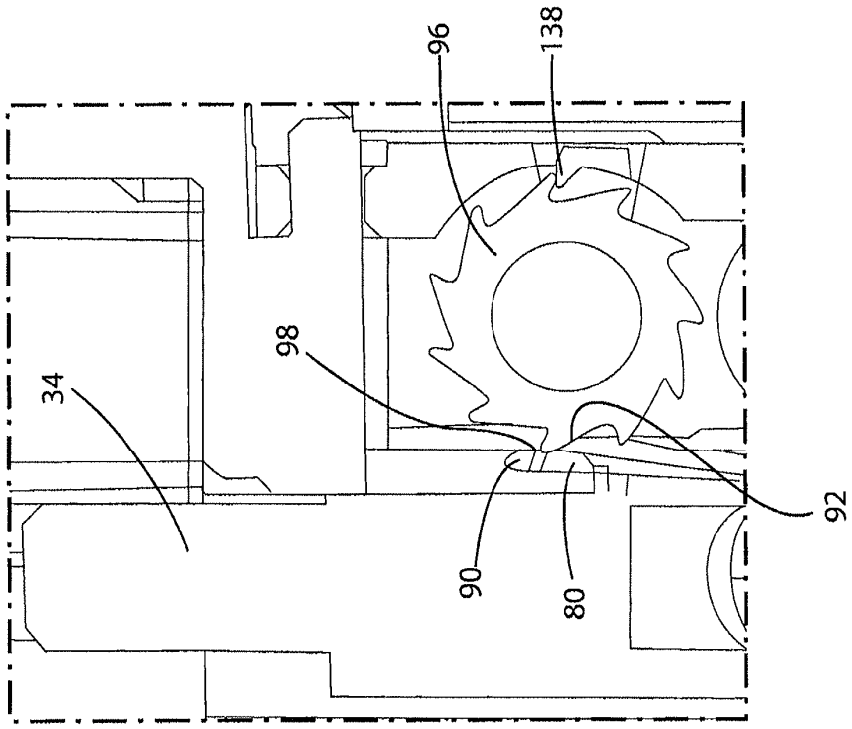


FIG. 10C

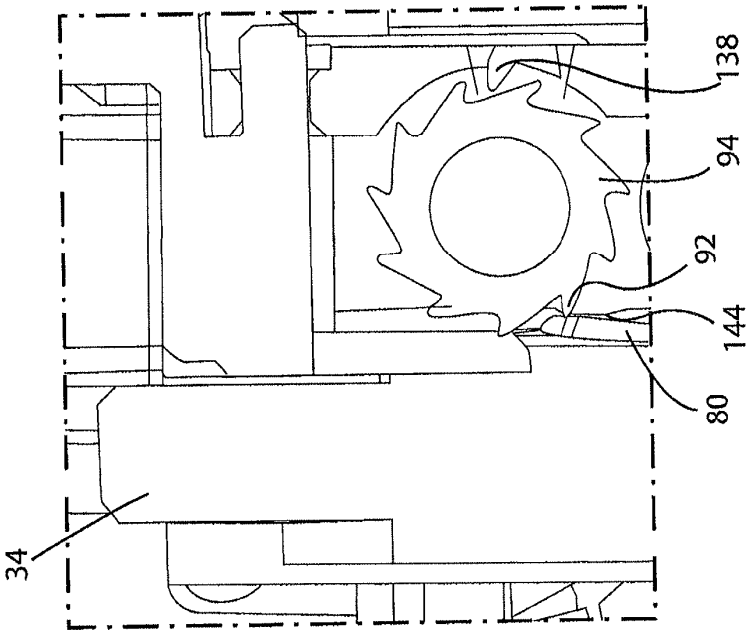


FIG. 10F

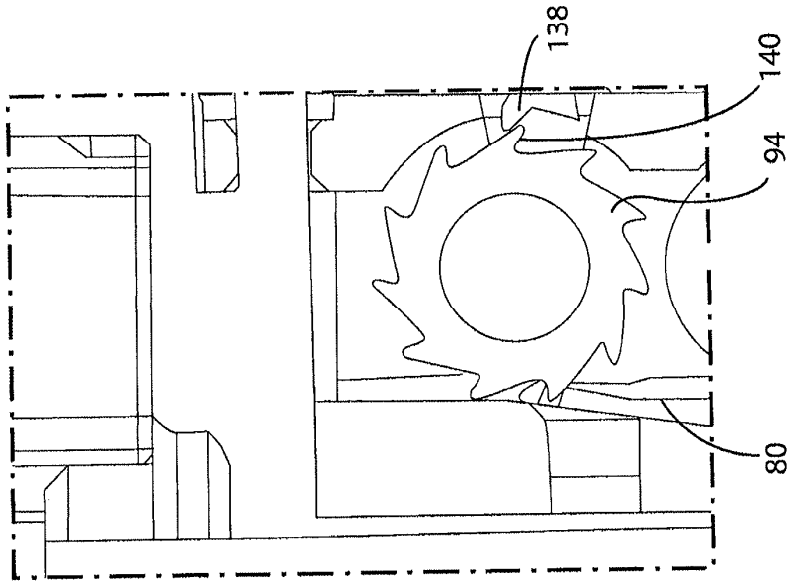


FIG. 10D

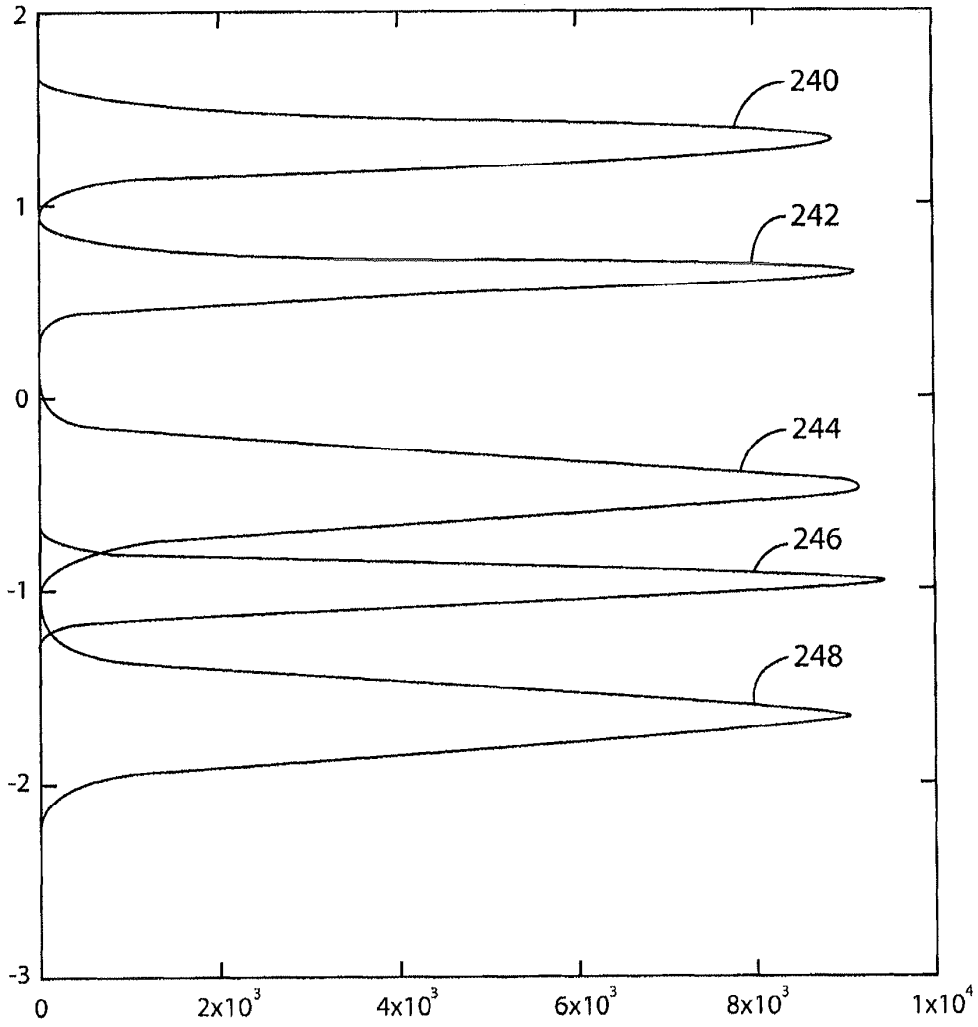

2
1
0
-1
-2
-3
240
242
244
246
248
0
2x10^3
4x10^3
6x10^3
8x10^3
1x10^4

FIG. 11

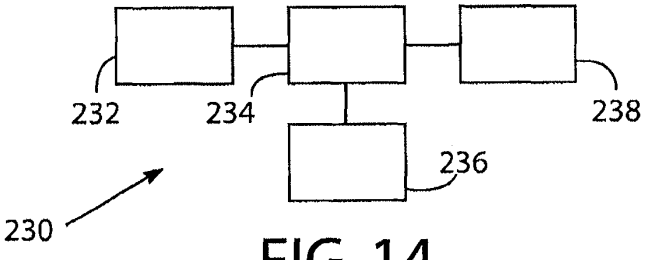

232
234
238
236
230

FIG. 14

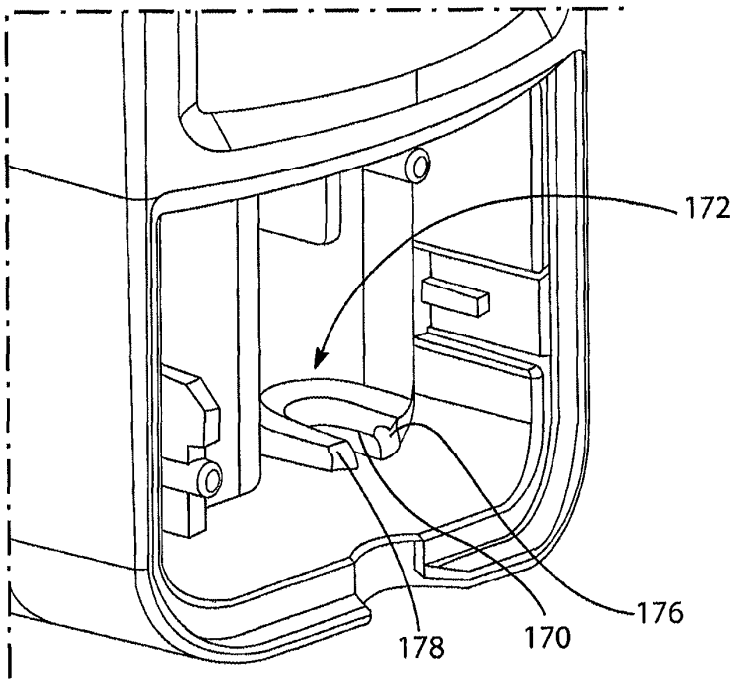


FIG. 12

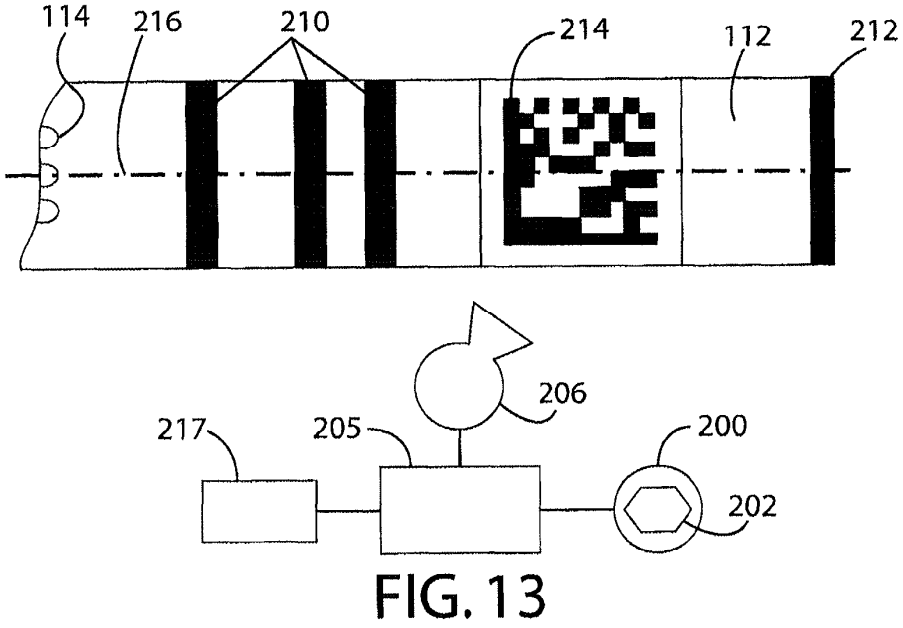


FIG. 13

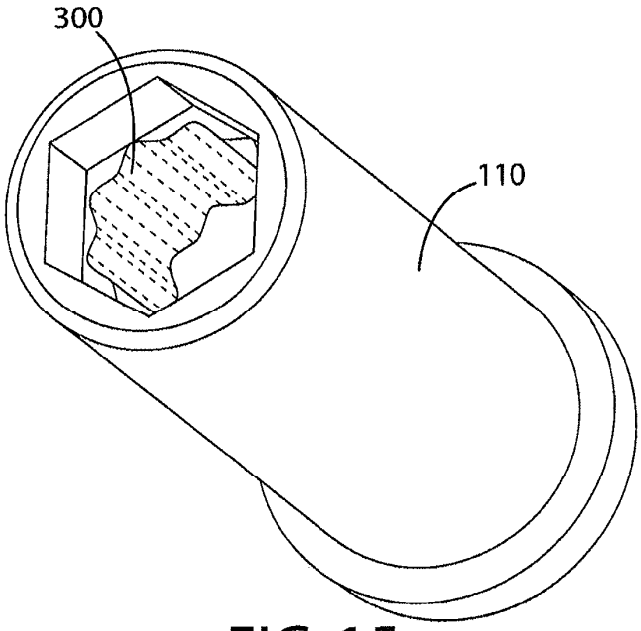


FIG. 15

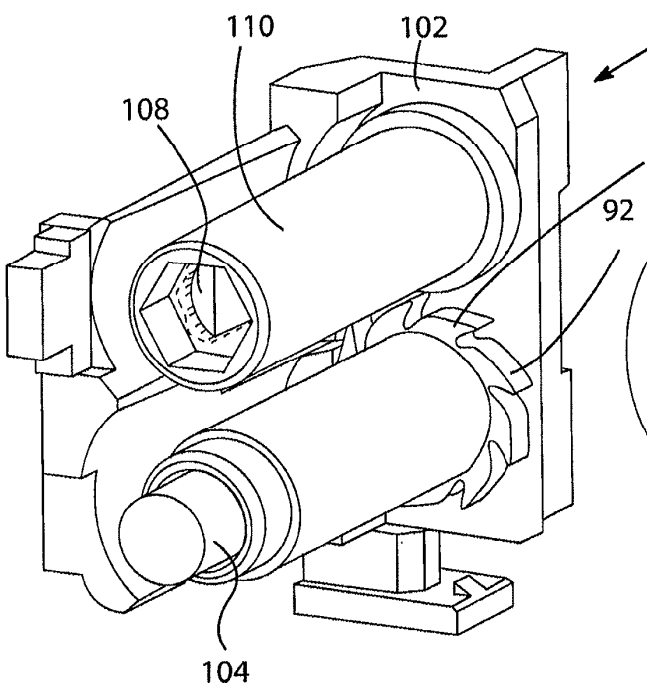


FIG. 20

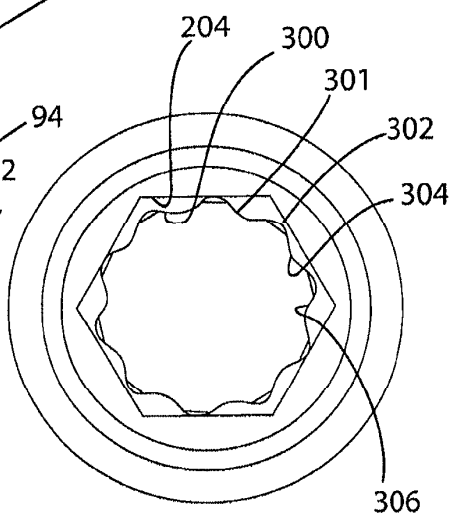


FIG. 16

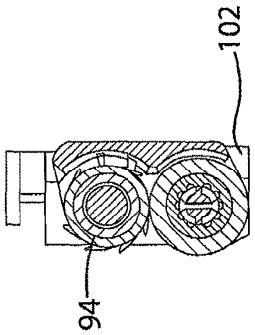


FIG. 19A

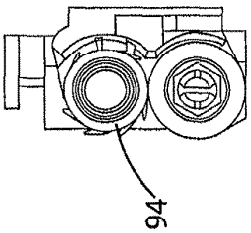


FIG. 19B

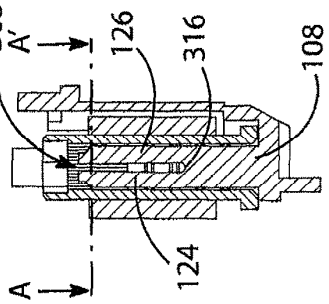


FIG. 19C

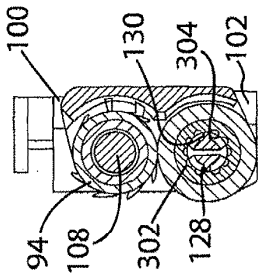


FIG. 18A

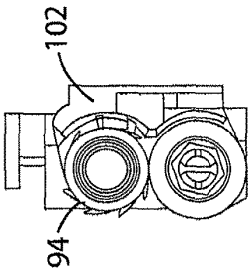


FIG. 18B

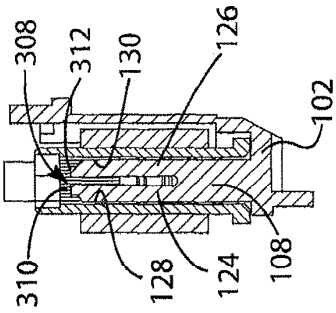


FIG. 18C

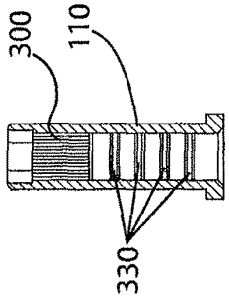


FIG. 17

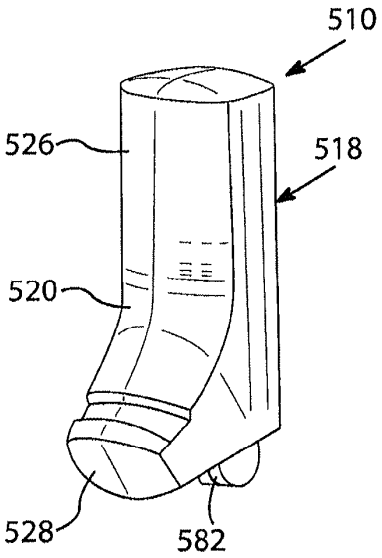

510
526
518
520
528
582

FIG. 21

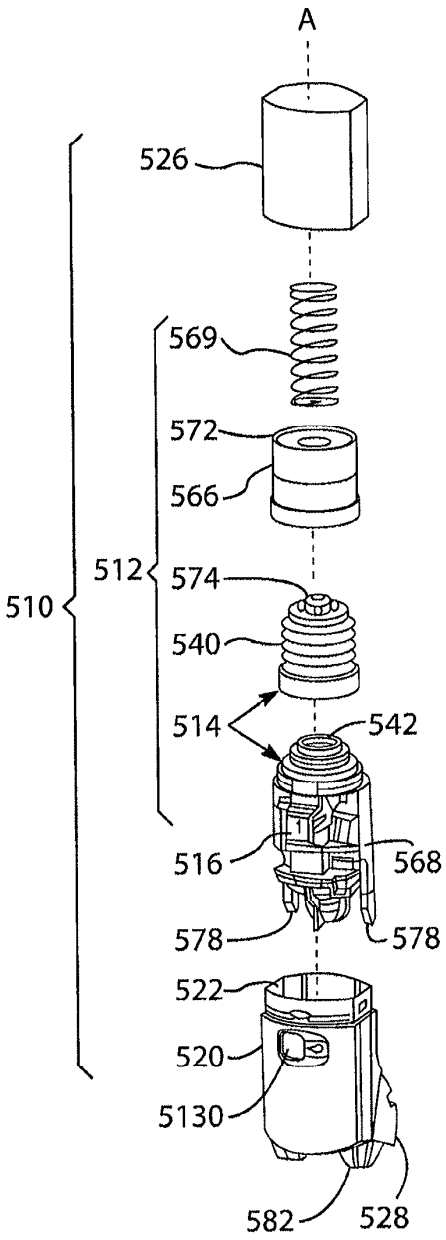

A
526
569
572
566
512
574
510
540
514
542
516
568
578
578
522
520
5130
582
528

FIG. 22

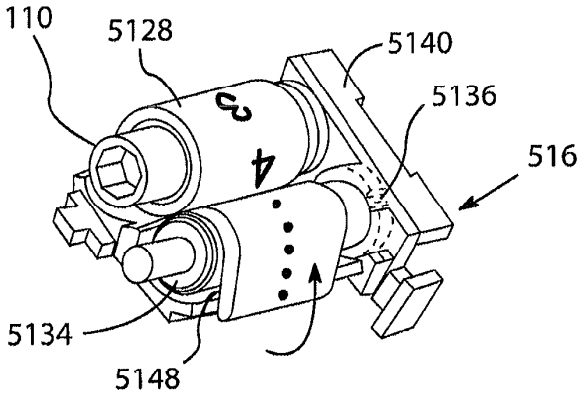

110
5128
5140
5136
516
5134
5148

FIG. 23

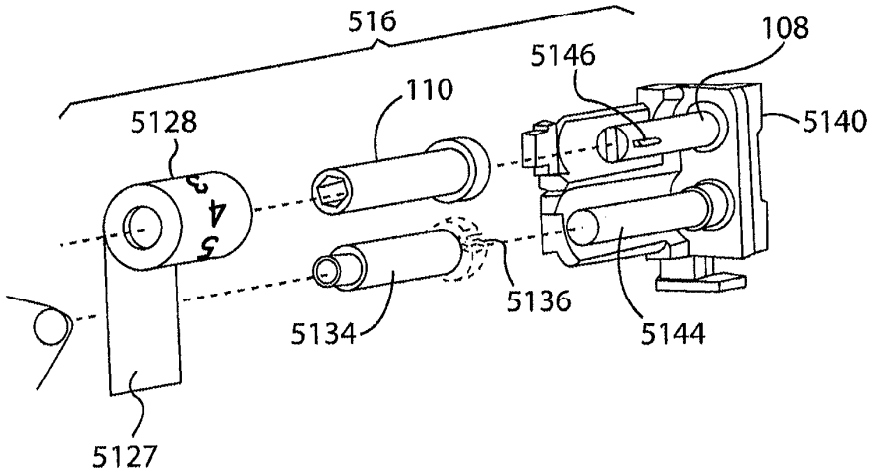

516
108
5146
110
5128
5140
5136
5134
5144
5127

FIG. 24

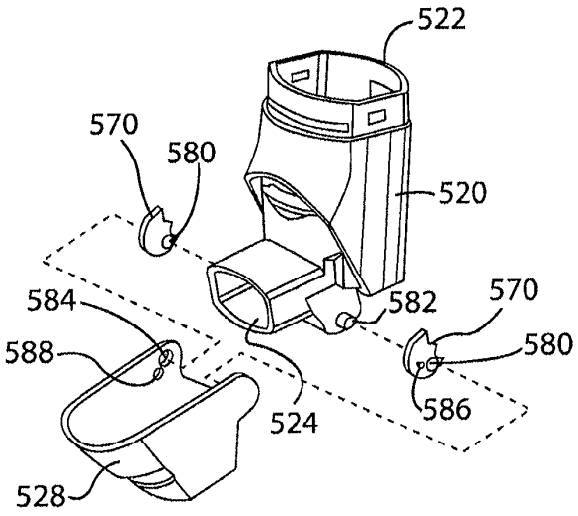


FIG. 25

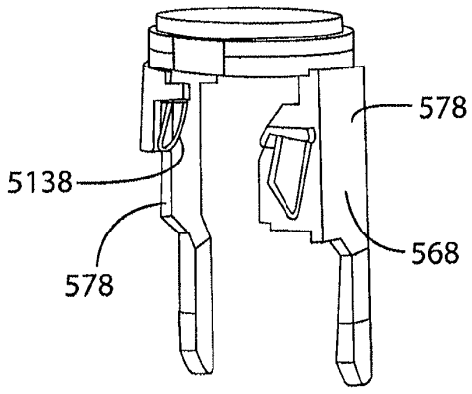


FIG. 26

DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation patent application of U.S. Non-Provisional patent application Ser. No. 14/699,584, filed Apr. 29, 2015, which is a continuation patent application of U.S. Non-Provisional patent application Ser. No. 14/103,353, filed Dec. 11, 2013, which is a divisional patent application of U.S. Non-Provisional patent application Ser. No. 13/110,532, filed May 18, 2011, now U.S. Pat. No. 8,978,966, issued Mar. 17, 2015, which claims priority to U.S. Provisional Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Provisional Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for any and all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-dawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler is closed. Due to the way in which the mouthpiece is opened and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/−0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections maybe provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is

arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an otherwise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf my also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is be highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is high advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter

display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia. The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. **1** is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. **2** is a top plan view of the components as shown in FIG. **1**;

FIG. **3**A is a section on the plane **3**A-**3**A in FIG. **2**;

FIG. **3**B is a view corresponding to FIG. **3**A but with a dose counter fitted to the main body of the inhaler;

FIG. **4**A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. **4**B is a view in the direction **4**B in FIG. **4**C of a spring retainer of the dose counter;

FIG. **4**C is a top view of the spring retainer of FIG. **4**B;

FIG. **5** is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. **6**A, **6**B, **6**C, **6**D, **6**E, **6**F, **6**G and **6**H are various views of dose counter components of the inhaler;

FIGS. **7**A and **7**B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. **7**C is a further sectional view similar to that of FIG. **7**B but with the canister removed;

FIG. **7**D is a top plan view of the inhaler main body;

FIGS. **8**A, **8**B, **8**C and **8**D show the inhaler main body and dose counter components during assembly thereof;

FIG. **9** shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. **10**A, **10**B, **10**C, **10**D, **10**E and **10**F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. **11** shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. **12** is an enlarged version of part of FIG. **4**A;

FIG. **13** shows an end portion of a tape of the dose counter;

FIG. **14** shows a computer system for designing the dose counter;

FIG. **15** is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. **1** to **14**;

FIG. **16** shows an end view of the stock bobbin of FIG. **15**;

FIG. **17** is a section through a longitudinal axis of the stock bobbin of FIGS. **15** and **16**;

FIGS. **18**A, **18**B and **18**C are views of the stock bobbin of FIGS. **15** to **17** mounted in the dose counter chassis of FIGS. **1** to **14**, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. **6**F, with the forks in a compressed configuration;

FIGS. **19**A, **19**B and **19**C are views equivalent to FIGS. **18**A to **18**C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. **20** is an isometric view of the chassis assembled and including the stock bobbin of FIGS. **15** to **17** but excluding the tape for reasons of clarity;

FIG. **21** is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. **22** is an exploded view of the inhaler of FIG. **21**;

FIG. **23** is a view of a dose counter of the inhaler of FIG. **21**;

FIG. **24** is an exploded view of the dose counter shown in FIG. **23**;

FIG. **25** is an exploded view of parts of the inhaler of FIG. **21**; and

FIG. **26** is a view of a yoke of the inhaler of FIG. **21**.

DETAILED DESCRIPTION OF THE INVENTION

FIG. **1** shows a main body **10** of a manually operated metered dose inhaler **12** in accordance with an embodiment related to the present invention and having a mouthpiece cap **14** securable over a mouthpiece **16** of the main body.

The main body has a canister chamber **18** into which a canister **20** (FIG. **7**A) is slideable. The canister **20** has a generally cylindrical main side wall **24**, joined by a tapered section **26** to a head portion **28** having a substantially flat lower face **30** which has an outer annular drive surface **32** arranged to engage upon and drive an actuation pin **34** of a dose counter **36** as will be described. Extending centrally and axially from the lower face **30** is a valve stem **38** which is arranged to sealingly engage in a valve stem block **40** of the main body **10** of the inhaler **12**. The valve stem block **40** has a passageway **42** leading to a nozzle **44** for directing the contents of the canister **20**, namely active drug and propellant, towards an air outlet **46** of the inhaler main body **12**. It will be appreciated that due to gaps **48** between the canister **20** and an inner wall **50** of the main body **10** of the inhaler **12** an open top **52** of the main body **10** forms an air inlet into the inhaler **12** communicating via air passageway **54** with the air outlet **46**, such that canister contents exiting nozzle **44** mix with air being sucked by the user through the air passageway **54** in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter **36** will now be described. The dose counter **36** includes an actuation pin **34** biased upwardly from underneath by a return spring **56** once installed in the main body **10**. As best shown in FIGS. **4**A, **6**H and **8**A, the pin **34** has side surfaces **58**, **60** arranged to slide between corresponding guide surfaces **62**, **64** located in a dose counter chamber **66** of the main body **10**, as well as an end stop surface **68** arranged to engage a corresponding end stop **70** formed in the dose counter chamber **66** to limit upward movement of the pin **34**. The pin **34** has a top part **72** which is circularly cylindrical and extends through an aperture **74** formed through a separator wall **76** which separates the canister chamber **18** from the dose counter chamber **66**. The top part **72** of the pin **34** has a flat top surface **78** which is arranged to engage the outer annular drive surface **32** of the canister **20**.

The actuation pin **34** is integrally formed with a drive or actuator pawl **80**. The actuator pawl **80** has a generally inverted U-shape configuration, having two mutually spaced and parallel arms **82**, **84** extending from a base portion of the actuation pin **34**, each holding at respective distal ends **88** thereof opposite ends of a pawl tooth member **90** which extends in a direction substantially perpendicular to the arms **82**, **84**, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth **92** of a ratchet wheel **94** of an incremental drive system **96** or ratchet mechanism **96** of the dose counter **36**. As shown for example in FIG. **10**B, the pawl tooth member **90** has a sharp lower

longitudinal side edge **98** arranged to engage the drive teeth **92**, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl **80** and resultant rotational positioning of the ratchet wheel **94**.

The dose counter **36** also has a chassis preassembly **100** which, as shown in FIGS. **4**A and **6**A, includes a chassis **102** having a first shaft **104** receiving the ratchet wheel **94** which is secured to a tape reel shaft **106**, and a second shaft (or split pin) **108** which is parallel to and spaced from the first shaft **104** and which slidably and rotationally receives a tape stock bobbin **110**.

As shown in FIG. **6**B, when the inhaler has not been used at all, the majority of a tape **112** is wound on the tape stock bobbin **110** and the tape **112** has a series of regularly spaced numbers **114** displayed therealong to indicate a number of remaining doses in the canister **20**. As the inhaler is repeatedly used, the ratchet wheel **94** is rotated by the actuator pawl **80** due to operation of the actuation pin **34** by the canister **20** and the tape **112** is incrementally and gradually wound on to the tape reel shaft **106** from the second shaft **108**. The tape **112** passes around a tape guide **116** of the chassis **102** enabling the numbers **114** to be displayed via a window **118** in a dose counter chamber cover **120** having a dose marker **132** formed or otherwise located thereon.

As shown in FIGS. **6**A and **6**D, the second shaft **108** is forked with two forks **124**, **126**. The forks **124**, **126** are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft **108** friction or control elements **128**, **130**, one on each fork. Each control element extends longitudinally along its respective fork **124**, **126** and has a longitudinally extending friction surface **132**, **134** which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore **136** inside the tape stock bobbin **110**. This control arrangement provided between the bore **136** and the control elements **128**, **130** provides good rotational control for the tape stock bobbin **110** such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin **110** and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. **6**D, as well as FIGS. **6**G and **10**A to **10**F, the chassis **102** is provided with an anti-back drive tooth **138** or count pawl **138** which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. **10**A to **10**F, when the actuation pin **34** is depressed fully so as to fire the metered valve (not shown) inside the canister **20**, the actuator pawl **80** pulls down on one of the teeth **92** of the ratchet wheel **94** and rotates the wheel **94** anticlockwise as shown in FIG. **6**D so as to jump one tooth **92** past the count pawl **138**, thereby winding the tape **112** a distance incrementally relative to the dose marker **122** on the dose counter chamber **120** so as to indicate that one dose has been used.

With reference to FIG. **10**B, the teeth of the ratchet wheel **94** have tips **143** which are radiused with a 0.1 mm radius between the flat surfaces **140**, **142**. The ratchet wheel **94** has a central axis **145** which is 0.11 mm above datum plane **220** (FIG. **9**). A top/nose surface **147** of the anti-back drive tooth **138** is located 0.36 mm above the datum plane **220**. The distance vertically (i.e. transverse to datum plane **220**—FIG. **9**) between the top nose surface **147** of the anti-back drive tooth is 0.25 mm from the central axis **145** of the wheel **94**. Bump surface **144** has a lateral extent of 0.20 mm, with a vertical length of a flat **145'** thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis **145**), the top **149** of the bump surface **144** being 3.02 mm vertically below the axis **145**, and the flat **145'** being spaced a distance sideways (i.e. parallel to the datum plane **220**) 2.48 mm from the axis **145**. The top surface **78** of the pin **34** (FIG. **6**H) is 11.20 mm above the datum plane **220** (FIG. **9**) when the actuator pawl **80** and pin **34** are in the start configuration. The length of the valve stem **22** is 11.39 mm and the drive surface **32** of the canister **20** is 11.39 mm above the datum plane **220** when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister **20** and the pin **34** in this configuration.

FIGS. **10**A and **10**B show the actuator pawl **80** and ratchet wheel **94** and count pawl **138** in a start position in which the flat top **78** of the pin **34** has not yet been engaged by the outer annular drive surface **32** of the canister **20** or at least has not been pushed down during a canister depression.

In this "start" position, the count pawl **138** engages on a non-return back surface **140** of one of the teeth **92** of the ratchet wheel **94**. The lower side edge **98** of the actuator pawl is a distance "D" (FIG. **9**) 1.33 mm above datum plane **220** which passes through bottom surface or shoulder **41** of valve stem block **40**, the datum plane **220** being perpendicular to a main axis "X" of the main body **10** of the inhaler **12** which is coaxial with the centre of the valve stem block bore **43** and parallel to a direction of sliding of the canister **20** in the main body **10** of the inhaler **12** when the canister is fired.

As shown in FIG. **10**B, an advantageous feature of the construction is that the pawl tooth/actuator **90** acts as a supplementary anti-back drive member when the inhaler **12** is not being used for inhalation. In particular, if the inhaler **12** is accidentally dropped, resulting in a jolt to the dose counter **36** then, if the wheel **94** would try to rotate clockwise (backwards) as shown in FIG. **10**B, the back surface **140** of a tooth will engage and be blocked by the tooth member **90** of the pawl **80**. Therefore, even if the anti-back drive tooth **138** is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel **94** is prevented and, upon the next canister firing sequence, the pawl **90** will force the wheel **94** to catch up to its correct position so that the dose counter **36** continues to provide correct dosage indication.

FIG. **10**C shows a configuration in which the actuator pawl **80** has been depressed with the pin **34** by the canister **20** to a position in which the side edge **98** of the pawl tooth member **90** is just engaged with one of the teeth **92** and will therefore upon any further depression of the pin **34** begin to rotate the wheel **94**. This is referred to as a "Reset" position or configuration. In this configuration, the lower side edge **98** of the actuator **80** is 0.64 mm above the datum plane **220**.

FIG. **10**D shows a configuration in which the actuator pawl **80** has been moved to a position lower than that shown in FIG. **10**C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle **44**. It will be noted that in this configuration the count pawl **138** is very slightly spaced from the back surface **140** of the same tooth **92** that it was engaging in the configuration of FIG. **10**D. The configuration shown in FIG. **10**D is known as a "Fire" configuration. In this configuration the lower side edge **98** of the actuator **80** is 0.47 mm below the datum plane **220**.

FIG. **10**E shows a further step in the sequence, called a "Count" position in which the actuator pawl **80** has rotated the ratchet wheel **94** by the distance circumferentially angularly between two of the teeth **92**, such that the count pawl **138** has just finished riding along a forward surface **142** of one of the teeth **92** and has resiliently jumped over the tooth

into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**. Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10**F, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6**G) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10**F will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10**F.

As shown in FIGS. **7**C and **7**D, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7**B a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7**A and schematically in FIG. **7**B, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** a as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails **144**, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7**C for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8**A, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8**B, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4**B, **4**C and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6**B) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6**B may as shown in FIG. **8**C be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8**D, the

dose counter chamber **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8**D being "200", thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8**D, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18**C and **19**C, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6**F. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radio extent of the control elements **128**, **130**, is 3.1 millimetres and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18**C and **19**C is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18**A to **18**C when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19**A to **19**C, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**

It will be appreciated that whereas FIGS. **18**B and **19**B are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18**A and **19**A are cross-sections. FIG. **19**A is a section on the plane A-A' in FIG. **19**C and FIG. **18**A is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

As the inhaler **12** is used and the ratchet wheel **94** rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin **108** at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin **108** at such rotational positions and this may involve a click forward of the stock bobbin **110** to the next position equivalent to that in FIGS. **19**A to **19**C in which the control elements **128**, **130** of the split pin art located in the concavities **302**. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape **112** from loosening during transit if the inhaler **12** is dropped, such as onto a hard surface. This is highly advantageous, since the tape **11** is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. **18**C and **19**C, the forks **124**, **126** rotate about a point **316** on the split pin where the forks **124**, **126** come together. This rotational action means that there is a camming action between the forks **124**, **126** and the engagement surface **300** without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface **300** and forks **124**, **126** are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler **12** is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape **112** to overcome the regulator at the stock bobbin **110**. 0.32 N is achieved with the control elements **128** having the profile shown in FIG. **19**C and 0.38 N is achieved with the profile of the control elements **128** altered to be as shown as described with reference to FIG. **6**F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. **15** to **20** does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape **112** as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape **112** can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities **302** and convex wall portions **304**, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements **128**, **130** are provided, so that all of the control elements **128**, **130** will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface **300** on the inside of the stock bobbin **110**, it could be placed on the outside of the stock bobbin **110** so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface **300** and forks **124**, **126** does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel **94**. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin **110** can be wound backwards during or after fitting the bobbin **100**, shaft **106** and tape **112** onto the carriage **102**, if desired.

The stock bobbin **110** and the carriage **102** including the split pin **108** are both moulded of polypropylene material.

It will be seen from FIG. **16** that the cross-sectional shape **301** is not symmetrical within the hexagonal socket **204**. This has enabled the hexagonal socket **204** to be maintained at a useful size while still allowing the desired size and geometry of the cross section **301** to fit without interfering with the hexagonal shape of the hexagonal socket **204** and also permits moulding to work during manufacture.

As shown in FIG. **17**, the stock bobbin **110** has a series of four circumferential ribs **330** inside it and a spaced thereabout. These hold the stock bobbin **110** on the correct side of the mould tool during moulding.

FIGS. **21** and **22** show a preferred embodiment in accordance with the invention of an inhaler **510** for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler **510** is as disclosed in FIGS. **1** to **16** or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin **110** and second shaft **108** of the dose counter **516** modified so as to be as in FIGS. **15** to **20** hereof. Thus, the dry powder inhaler **510** generally includes a housing **518**, and an assembly **512** received in the housing (see FIG. **21**). The housing **518** includes a case **520** having an open end **522** and a mouthpiece **524** (FIG. **25**) for patient inhalation, a cap **526** secured to and closing the open end **522** of the case **520**, and a cover **528** pivotally mounted to the case **520** for covering the mouthpiece **524**. As shown in FIG. **22**, the inhaler **510** also includes an actuation spring **569**, first yoke **566** with opening **572**, bellows **540** with crown **574**, a reservoir **514**, second yoke **568** with hopper **542** and dose counter **516** mounted thereto, and case **520** has transparent window **5130** thereon for viewing dose counter tape indicia **5128**. The dose metering system also includes two cams **570** mounted on the mouthpiece cover **528** and movable with the cover **528** between open and closed positions. The cams **570** each include an opening **580** for allowing outwardly extending hinges **582** of the case **520** to pass therethrough and be received in first recesses **584** of the cover **528**. The cams **570** also include bosses **586** extending outwardly and received in second recesses **588** of the cover **528**, such that the cover **528** pivots about the hinges **582** and the cams **570** move with the cover **528** about the hinges **582**. As described in EP-A-1330280, cams **570** act upon cam followers **578** to move second yoke **568** up and down and thereby operate dose counter by engagement of pawl **5138** on the second yoke **568** with teeth **5136**. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system **516** therefore includes a ribbon or tape **5128** (FIGS. **23** & **24**), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window **5130** provided in the housing **18** (see FIG. **22**). The dose counting system **516** includes the rotatable stock bobbin **110** (as described above), an indexing spool **5134** rotatable in a single direction, and the ribbon **5128** rolled and received on the bobbin **110** and having a first end **5127** secured to the spool **5134**, wherein the ribbon **5128** unrolls from the bobbin **110** so that the indicia are successively displayed as the spool **5134** is rotated or advanced. In FIGS. **23** and **24** the wavelike engagement surface **300** of the bobbin **110** is not shown for the purposes of clarity.

The spool **134** is arranged to rotate upon movement of the yokes **566**, **568** to effect delivery of a dose of medicament from reservoir **514**, such that the number on the ribbon **5128** is advanced to indicate that another dose has been dispensed by the inhaler **510**. The ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase or

decrease upon rotation of the spool **5134**. For example, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool **5134** to indicate the number of doses remaining in the inhaler **510**. Alternatively, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool **5134** to indicate the number of doses dispensed by the inhaler **10**.

The indexing spool **5134** includes radially extending teeth **5136**, which are engaged by pawl **5138** extending from a cam follower **578** of the second yoke **568** upon movement of the yoke to rotate, or advance, the indexing spool **5134**. More particularly, the pawl **5138** is shaped and arranged such that it engages the teeth **5136** and advances the indexing spool **5134** only upon the mouthpiece cover **528** being closed and the yokes **566**, **568** moved back towards the cap **526** of the housing **518**.

The dose counting system **516** also includes a chassis **5140** that secures the dose counting system to the hopper **542** and includes shafts **108**, **5144** for receiving the bobbin **110** and the indexing spool **5134**. As described above with reference to FIGS. **1** to **20**, the bobbin shaft **108** is forked and includes radially nubs **5146** for creating a resilient resistance to rotation of the bobbin **110** on the shaft **108** by engaging with the wavelike engagement surface **300** inside the bobbin **110**. A clutch spring **5148** is received on the end of the indexing spool **5134** and locked to the chassis **5140** to allow rotation of the spool **5134** in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed is:

1. A dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

2. The dose counter as claimed in claim **1** in which the counter display comprises a tape.

3. The dose counter as claimed in claim **2** in which the tape has dose counter indicia displayed thereon.

4. The dose counter as claimed in claim **2** wherein the first station comprises a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

5. The dose counter as claimed in claim **4** in which the first shaft is mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

6. The dose counter as claimed in claim **5** in which the regulator comprises at least one projection on one of the first shaft and the substantially rotationally fixed element, which is arranged to engage incrementally with one or more formations on the other of the substantially rotationally fixed element and the first shaft.

7. The dose counter as claimed in claim **6** in which at least two said projections are provided.

8. The dose counter as claimed in claim **6** in which exactly two said projections are provided.

9. The dose counter as claimed in claim **6** in which each projection comprises a radiused surface.

10. The dose counter as claimed in claim **6** in which the at least one projection is located on the substantially rotationally fixed element which comprises a fixed shaft which is fixed to the main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

11. The dose counter as claimed in claim **10** in which the fixed shaft has at least two flexible legs, and each leg has at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations.

12. The dose counter as claimed in claim **10** in which the fixed shaft comprises a split pin with fork legs and in which each projection is located on a said fork leg.

13. The dose counter as claimed in claim **6** in which a series of said formations are provided.

14. The dose counter as claimed in claim **6** in which an even number of said formations is provided.

15. The dose counter as claimed in claim **6** in which from eight to twelve of said formations are provided.

16. The dose counter as claimed in claim **15** in which ten of said formations are provided.

17. The dose counter as claimed in claim **6** in which each said formation comprises a concavity formed on an engagement surface.

18. The dose counter as claimed in claim **17** in which each concavity comprises a radiused surface wall portion which merges on at least one side thereof into a flat wall portion surface.

19. The dose counter as claimed in claim **18** in which the engagement surface includes a series of said concavities and in which convex wall portions of the engagement surface are formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

20. The dose counter as claimed in claim **19** in which each convex radiused wall portion of each convex wall portion is connected by said flat wall portion surfaces to each concavity which is adjacent thereto.

21. The dose counter as claimed in claim **4** in which the first shaft comprises a substantially hollow bobbin.

22. The dose counter as claimed in claim **21** in which said one or more formations are located on an inner surface of the bobbin.

23. The dose counter as claimed in claim **4** wherein the drive system comprises a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

24. The dose counter as claimed in claim **23** in which the second shaft is located on the main body of the dose counter spaced from and parallel to the first shaft.

25. The dose counter as claimed in claim **23** in which the tooth ratchet wheel is fixed to the second shaft and is arranged to rotate therewith.

26. The dose counter as claimed in claim **23** which includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

27. The dose counter as claimed in claim **1** in which the regulator provides a resistance force of greater than 0.1 N against movement of the counter display.

28. The dose counter as claimed in claim **27** in which the resistance force is greater than 0.3 N.

29. The dose counter as claimed in claim **27** in which the resistance force is from 0.3 to 0.4 N.

* * * * *

Exhibit E

US011395889B2

(12) **United States Patent**
Walsh et al.

(10) **Patent No.: US 11,395,889 B2**
(45) **Date of Patent: Jul. 26, 2022**

(54) **DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR**

(71) Applicants: **Ivax Pharmaceuticals Ireland**, Waterford (IE); **Norton (Waterford) Limited**, Waterford (IE); **Teva Pharmaceuticals Ireland**, Waterford (IE)

(72) Inventors: **Declan Walsh**, County Kilkenny (IE); **Derek Fenlon**, County Wexford (IE); **Simon Kaar**, County Cork (IE); **Jan Geert Hazenberg**, County Kilkenny (IE); **Daniel Buck**, County Waterford (IE); **Paul Clancy**, Waterford (IE); **Robert Charles Uschold**, Leominster, MA (US); **Jeffrey A. Karg**, Hopkinton, MA (US)

(73) Assignees: **Ivax Pharmaceuticals Ireland**, Waterford (IE); **Norton (Waterford) Limited**, Waterford (IE); **Teva Pharmaceuticals Ireland**, Waterford (IE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **16/915,558**

(22) Filed: **Jun. 29, 2020**

(65) **Prior Publication Data**

US 2021/0016026 A1 Jan. 21, 2021

Related U.S. Application Data

(60) Continuation of application No. 15/804,735, filed on Nov. 6, 2017, now Pat. No. 10,695,512, which is a continuation of application No. 15/269,249, filed on Sep. 19, 2016, now Pat. No. 9,808,587, which is a continuation of application No. 14/103,324, filed on Dec. 11, 2013, now Pat. No. 9,463,289, which is a division of application No. 13/110,532, filed on May 18, 2011, now Pat. No. 8,978,966.

(Continued)

(51) **Int. Cl.**
A61M 15/00 (2006.01)
G06M 1/24 (2006.01)
A61M 11/00 (2006.01)

(52) **U.S. Cl.**
CPC ***A61M 15/0078*** (2014.02); ***A61M 11/00*** (2013.01); ***A61M 15/007*** (2014.02);
(Continued)

(58) **Field of Classification Search**
CPC A61M 15/0078; A61M 15/0025; A61M 15/0026; A61M 15/007; A61M 15/0071;
(Continued)

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,174,890 A 11/1979 Johnson
4,669,838 A 6/1987 Hibbard
(Continued)

FOREIGN PATENT DOCUMENTS

CA 2501726 9/2006
CN 1265601 9/2000
(Continued)

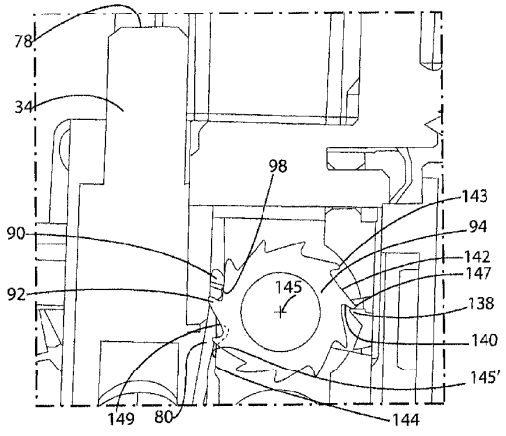
OTHER PUBLICATIONS

Advisory Action dated Mar. 13, 2017 for U.S. Appl. No. 14/699,567.
(Continued)

Primary Examiner — Daniel A Hess
(74) *Attorney, Agent, or Firm* — Morgan, Lewis & Bockius LLP

(57) **ABSTRACT**

An inhaler includes a main body having a canister housing, a medicament canister retained in a central outlet port of the canister housing, and a dose counter having an actuation member for operation by movement of the medicament canister. The canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall. The canister housing
(Continued)



has a longitudinal axis X which passes through the center of the central outlet port. The first inner wall canister support formation, the actuation member, and the central outlet port lie in a common plane coincident with the longitudinal axis X such that the first inner wall canister support formation protects against unwanted actuation of the dose counter by reducing rocking of the medicament canister relative to the main body of the inhaler.

6 Claims, 17 Drawing Sheets

Related U.S. Application Data

(60) Provisional application No. 61/417,659, filed on Nov. 29, 2010, provisional application No. 61/345,763, filed on May 18, 2010.

(52) **U.S. Cl.**
CPC ***A61M 15/009*** (2013.01); ***A61M 15/0025*** (2014.02); ***A61M 15/0026*** (2014.02); ***A61M 15/0065*** (2013.01); ***A61M 15/0071*** (2014.02); ***G06M 1/246*** (2013.01); *A61M 2202/064* (2013.01); *A61M 2205/6063* (2013.01); *A61M 2207/00* (2013.01); *A61M 2207/10* (2013.01); *Y10T 29/49* (2015.01); *Y10T 29/49764* (2015.01); *Y10T 29/49826* (2015.01)

(58) **Field of Classification Search**
CPC A61M 11/00; A61M 15/0065; A61M 15/009; G06M 1/246
USPC 128/203.12
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,687,359	A	8/1987	Barrus	
5,349,945	A	9/1994	Wass et al.	
5,482,030	A	1/1996	Klein	
5,861,911	A	1/1999	Oosaka	
6,142,339	A	11/2000	Blacker et al.	
6,446,627	B1 *	9/2002	Bowman	A61M 15/009 128/200.23
6,659,307	B1	12/2003	Stradella	
6,718,972	B2	4/2004	OLeary	
6,907,876	B1	6/2005	Clark et al.	
7,107,986	B2	9/2006	Rand et al.	
7,156,258	B2	1/2007	Eckert	
7,587,988	B2	9/2009	Bowman et al.	
7,661,423	B2	2/2010	Brand et al.	
7,819,075	B2	10/2010	Bowman et al.	
7,832,351	B2	11/2010	Bonney et al.	
8,418,690	B2	4/2013	Power	
8,459,253	B2	6/2013	Howgill	
8,474,448	B2	7/2013	Oi	
8,511,302	B2	8/2013	Parkes	
8,662,381	B2	3/2014	Kaar et al.	
8,978,966	B2	3/2015	Walsh et al.	
9,174,013	B2	11/2015	Walsh et al.	
9,216,261	B2	12/2015	Kaar et al.	
9,265,901	B2	2/2016	Lawrence et al.	
9,463,289	B2	10/2016	Walsh et al.	
9,533,111	B2	1/2017	Walsh et al.	
9,737,674	B2	8/2017	Walsh et al.	
9,808,587	B2	11/2017	Walsh et al.	
2002/0047021	A1	4/2002	Blacker	
2002/0078949	A1	6/2002	OLeary	
2002/0078950	A1	6/2002	OLeary	
2002/0084891	A1	7/2002	Mankins et al.	
2003/0209239	A1	11/2003	Rand	
2004/0089298	A1	5/2004	Haikarainen et al.	
2004/0095746	A1	5/2004	Murphy	
2005/0028815	A1	2/2005	Deaton	
2005/0087191	A1	4/2005	Morton	
2005/0126469	A1	6/2005	Lu	
2006/0096594	A1	5/2006	Bonney	
2006/0107949	A1	5/2006	Davies	
2006/0107979	A1	5/2006	Kim	
2007/0062518	A1	3/2007	Geser	
2007/0240712	A1	10/2007	Fleming et al.	
2007/0241025	A1	10/2007	Parkes	
2007/0246042	A1	10/2007	Purkins	
2008/0035144	A1	2/2008	Bowman et al.	
2008/0156321	A1	7/2008	Bowman et al.	
2008/0242465	A1	10/2008	Strobel	
2009/0178678	A1	7/2009	OLeary	
2010/0078490	A1	4/2010	Fenlon	
2010/0089395	A1	4/2010	Power	
2010/0218759	A1	9/2010	Anderson	
2011/0041845	A1	2/2011	Solomon	
2012/0006322	A1	1/2012	Anderson	
2012/0247458	A1	10/2012	Lawrence et al.	

FOREIGN PATENT DOCUMENTS

CN	1956448		5/2007
CN	101198972		6/2008
EP	1330280		7/2003
EP	1486227		12/2004
GB	2320489		6/1998
GB	2348928		10/2001
IL	201256		11/2014
JP	02502129		7/1990
JP	450059		8/1992
JP	07100205		4/1995
JP	10504220		4/1998
JP	2002528144		9/2002
JP	2004501685		1/2004
JP	2007534378		11/2007
JP	2008-94103	A	4/2008
JP	2008094103		4/2008
JP	2008261423		10/2008
JP	2009233308		10/2009
JP	2009257392		11/2009
JP	2010096308		4/2010
WO	8909078		10/1989
WO	9209324		6/1992
WO	9628205		9/1996
WO	9828033		7/1998
WO	9856444		12/1998
WO	9936115		7/1999
WO	01/28887		4/2001
WO	2001087391		11/2001
WO	02/00281	A2	1/2002
WO	03101514		12/2003
WO	2005060535		7/2005
WO	2005060917		7/2005
WO	2005102430		11/2005
WO	2006062449		6/2006
WO	2006062449	A1	6/2006
WO	2006110080		10/2006
WO	2007012861		2/2007
WO	2007062518		6/2007
WO	2008023019		2/2008
WO	2008119552		2/2008
WO	2008121459		10/2008
WO	2011012325		2/2011
WO	2011012327		2/2011

OTHER PUBLICATIONS

English Translation of Chinese Office Action, corresponds to CN201080041218.1.
English Translation of Chinese Office Action, corresponds to CN201080040988.4.
European Search report for EP Application No. 13004775.6.
European Search report for EP Application No. 13005367.1.
File History for U.S. Appl. No. 14/713,633.

(56) **References Cited**

OTHER PUBLICATIONS

Final OA for U.S. Appl. No. 13/387,532.
Final OA for U.S. Appl. No. 14/876,190.
International Search Report for PCT/EP10/04790.
International Search Report for PCT/EP10/04791.
International Search Report for PCT/EP10/04792.
Office Action issued by the Israel Patent Office dated Jul. 3, 2017 in reference to Israel Patent Application No. 247396, 3 pages.
Office Action issued by the Israel Patent Office dated Jul. 27, 2017 in reference to Israel Patent Application No. 247402, 4 pages.
Final Office Action dated Oct. 20, 2016 for U.S. Appl. No. 14/699,567.
Non-Final Office Action dated Jan. 12, 2017 for U.S. Appl. No. 14/713,620, 8 pages.
Final Rejection dated Sep. 27, 2016 for U.S. Appl. No. 14/699,578.
Final Office Action dated Aug. 31, 2016 for U.S. Appl. No. 14/713,620, 7 pages.
Advisory action dated Feb. 9, 2017 for U.S. Appl. No. 14/699,584.
Non-final rejection dated Jul. 12, 2016 for U.S. Appl. No. 14/713,643.
File History for U.S. Appl. No. 15/271,738.
File History for U.S. Appl. No. 15/269,102.
File History for U.S. Appl. No. 15/262,818.
File History for U.S. Appl. No. 15/289,553.
File History for U.S. Appl. No. 15/269,249.
Final rejection dated Oct. 20, 2016 or U.S. Appl. No. 14/699,584.
Non-Final Office Action dated Jun. 24, 2016 for U.S. Appl. No. 14/713,620, 7 pages.
Final rejection dated Oct. 20, 2016 or U.S. Appl. No. 14/713,633.
Advisory Action dated Mar. 16, 2017 or U.S. Appl. No. 14/713,633.
Entire patent prosecution history of U.S. Appl. No. 13/110,532, filed, May 18, 2011, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,324, filed, Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,343, filed, Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,353, filed, Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,363, filed, Dec. 1, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/103,392, filed, Dec. 11, 2013, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/699,567, filed, Apr. 29, 2015, entitled, "Dose Counter for Inhaler and Method for Counting Doses.".
Entire patent prosecution history of U.S. Appl. No. 14/699,578, filed, Apr. 29, 2015, entitled, "Dose Counter for Inhaler Having a Bore !And Shaft Arrangement.".
Entire patent prosecution history of U.S. Appl. No. 14/699,584, filed, Apr. 29, 2015, entitled, "Dose Counter for Inhaler Having an Antireverse Rotation Actuator.".
Entire patent prosecution history of U.S. Appl. No. 14/713,612, filed, May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/713,620, filed, May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
Entire patent prosecution history of U.S. Appl. No. 14/713,643, filed, May 15, 2015, entitled, "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof.".
European Patent Office Communication, dated Apr. 24, 2014 of counterpart European Patent Application No. 11 010 211.8.
European Patent Office Communication, dated Apr. 24, 2014 of counterpart European Patent Application No. 11 010 212.6.
First Examination Report of counterpart New Zealand Patent Application No. 603466, dated Jul. 1, 2013.
File history for U.S. Appl. No. 13/387,508.
File history for U.S. Appl. No. 13/387,532.
File history for U.S. Appl. No. 13/388,535.
File history for U.S. Appl. No. 14/132,918.
File history for U.S. Appl. No. 14/876,190.
File history for U.S. Appl. No. 14/967,905.
Office Action, Israel Application No. IL263904 dated Sep. 14, 2021, 4 pgs.

* cited by examiner

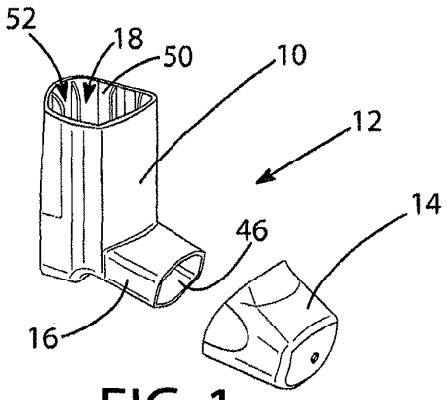


FIG. 1

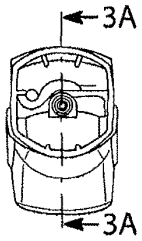


FIG. 2

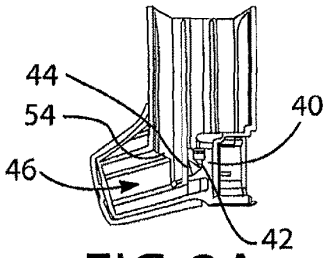


FIG. 3A

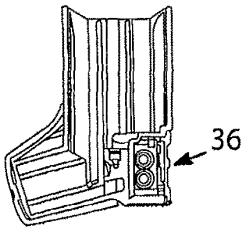


FIG. 3B

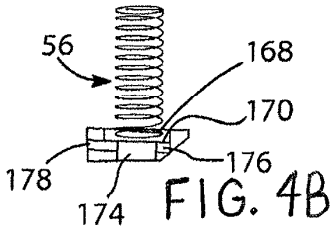


FIG. 4B

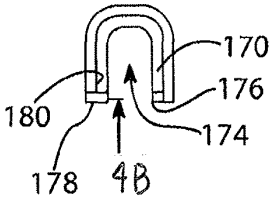


FIG. 4C

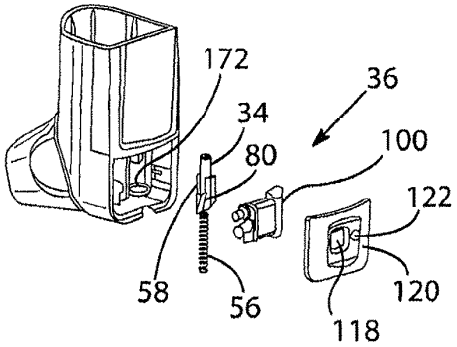


FIG. 4A

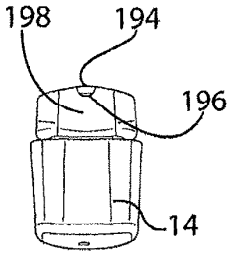


FIG. 5

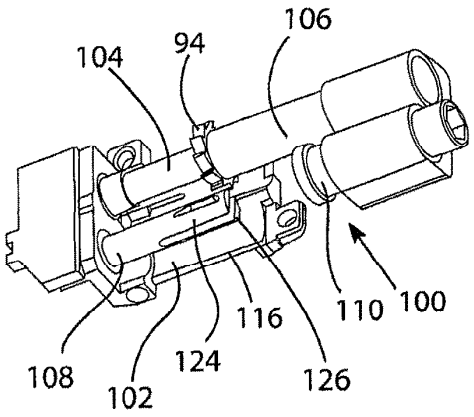


FIG. 6A

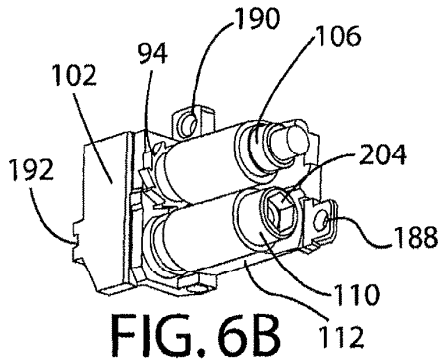


FIG. 6B

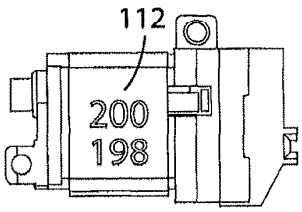


FIG. 6C

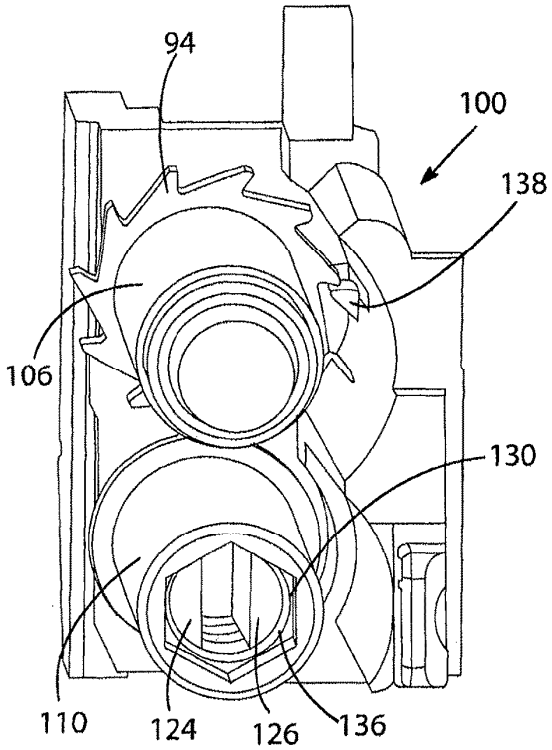


FIG. 6D

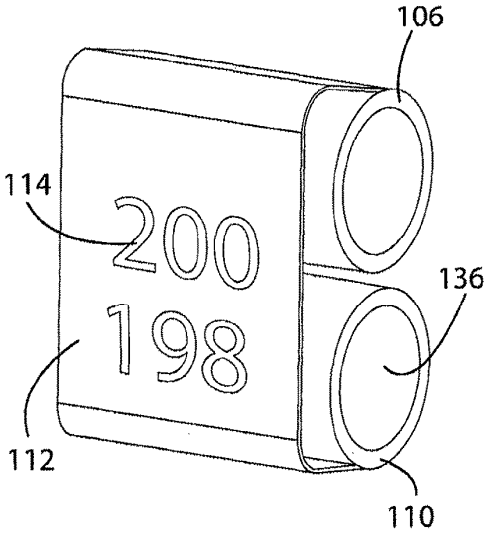


FIG. 6E

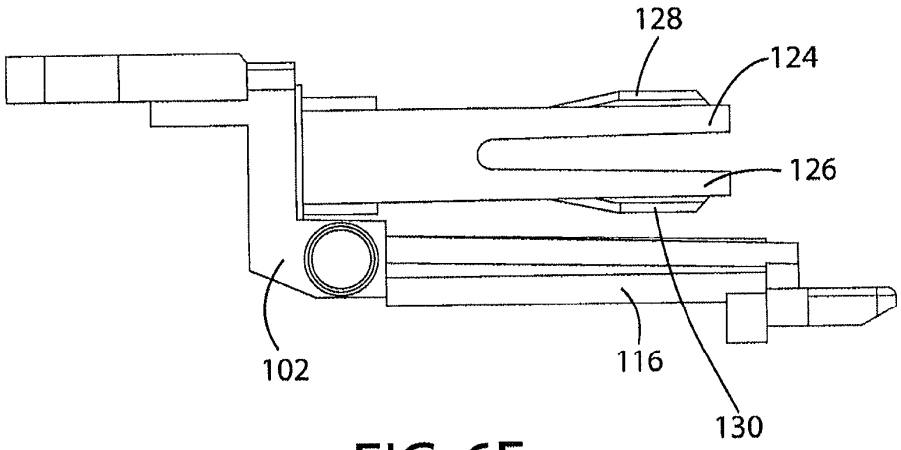


FIG. 6F

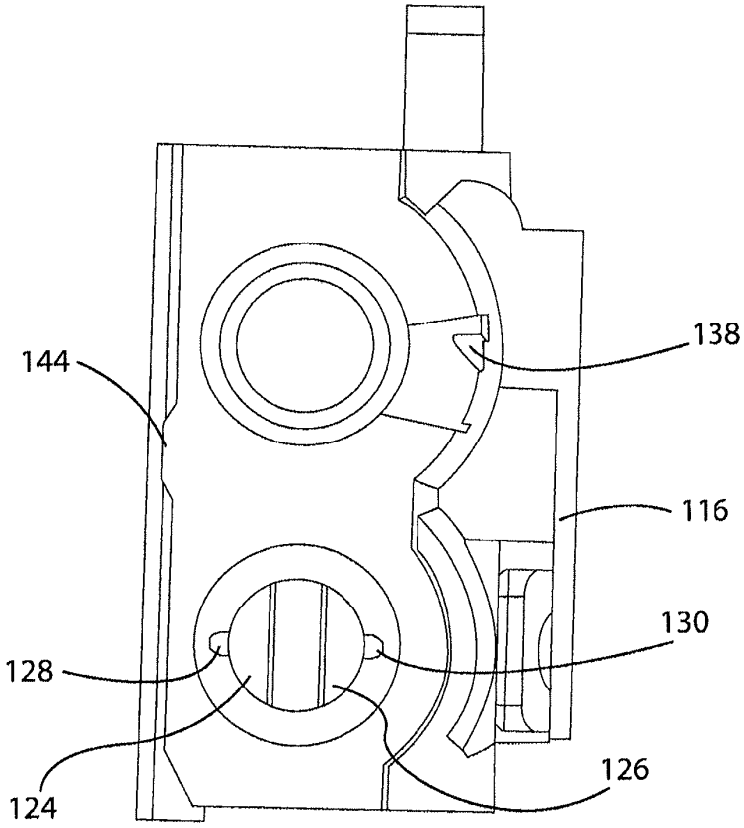


FIG. 6G

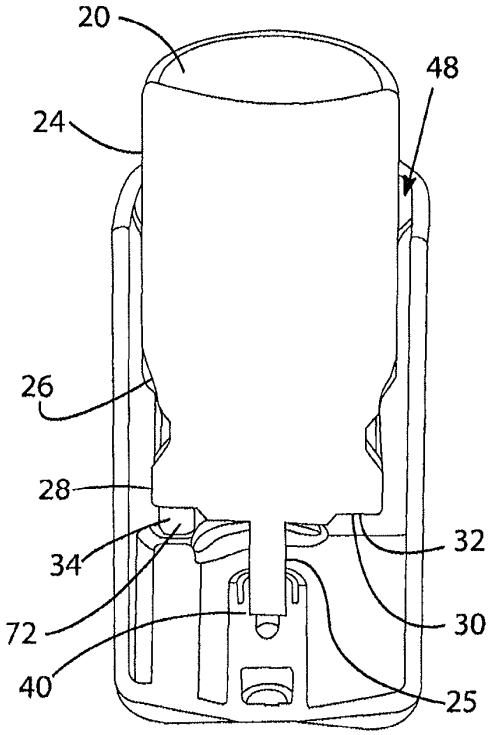


FIG. 7A

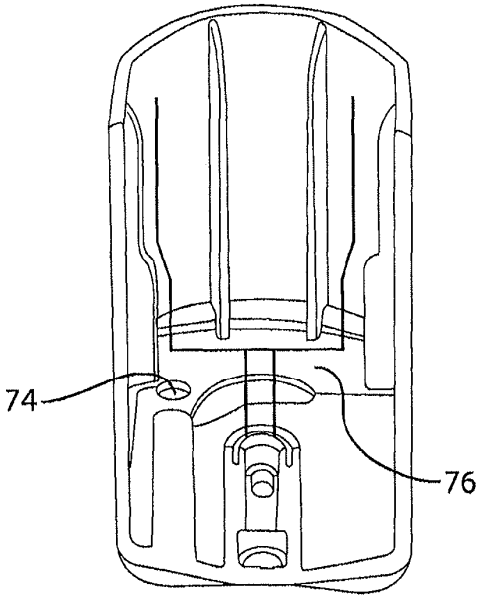


FIG. 7B

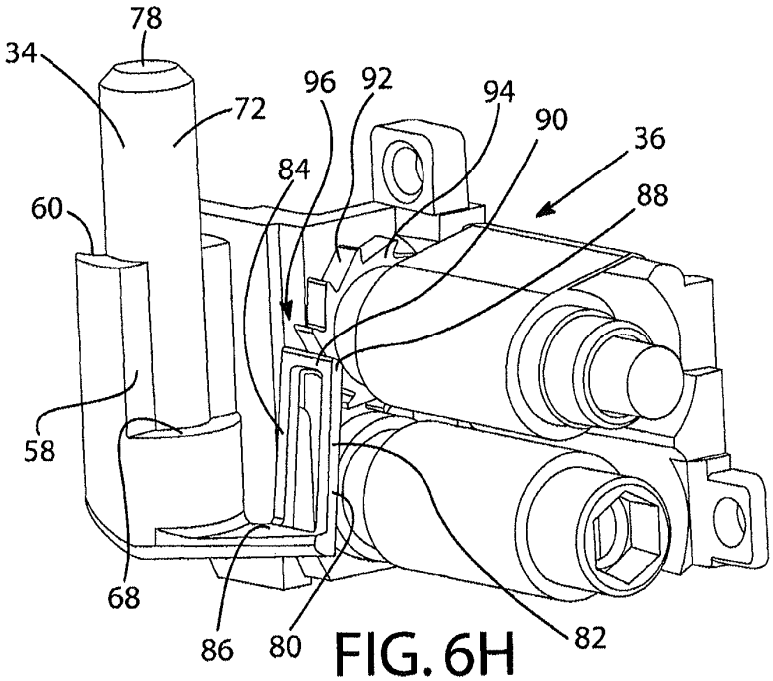


FIG. 6H

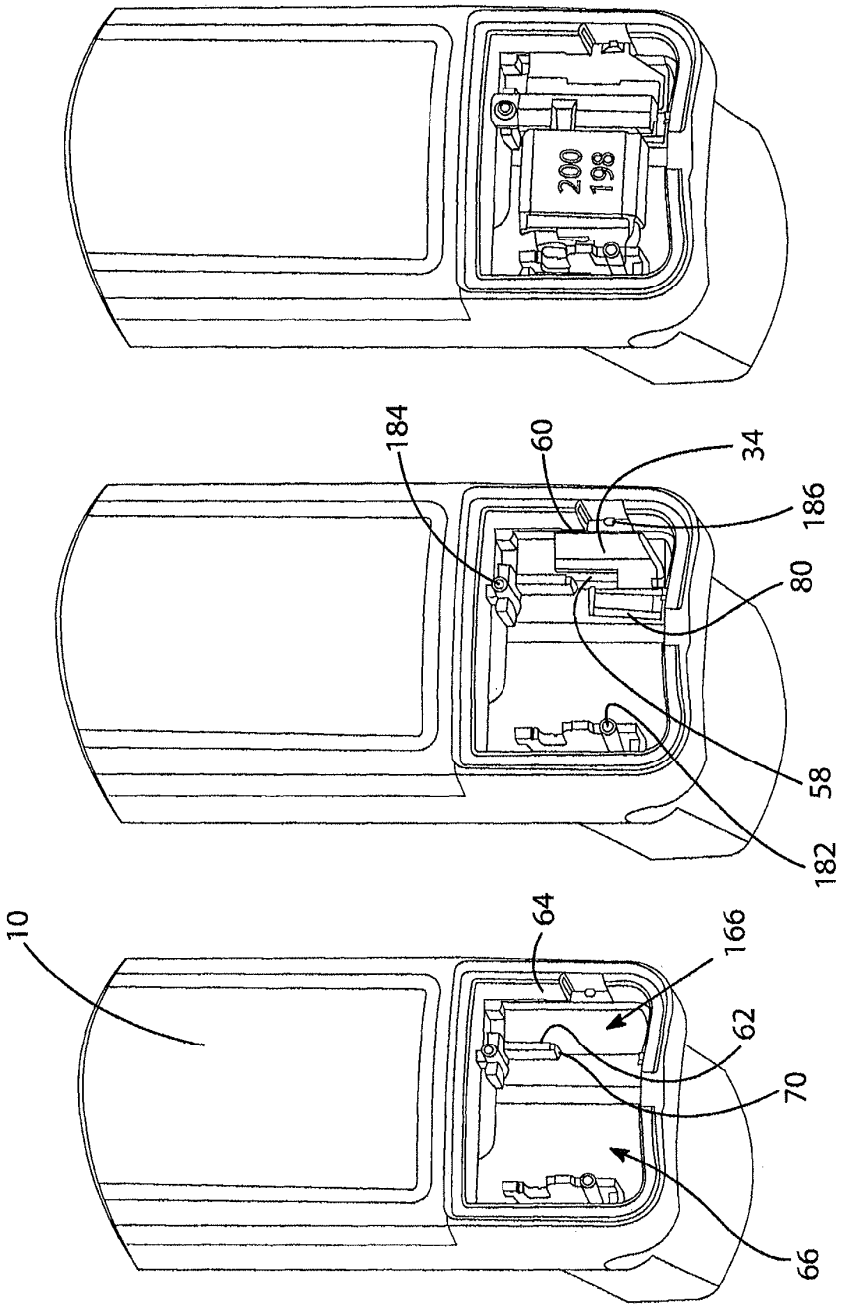


FIG. 8C

FIG. 8B

FIG. 8A

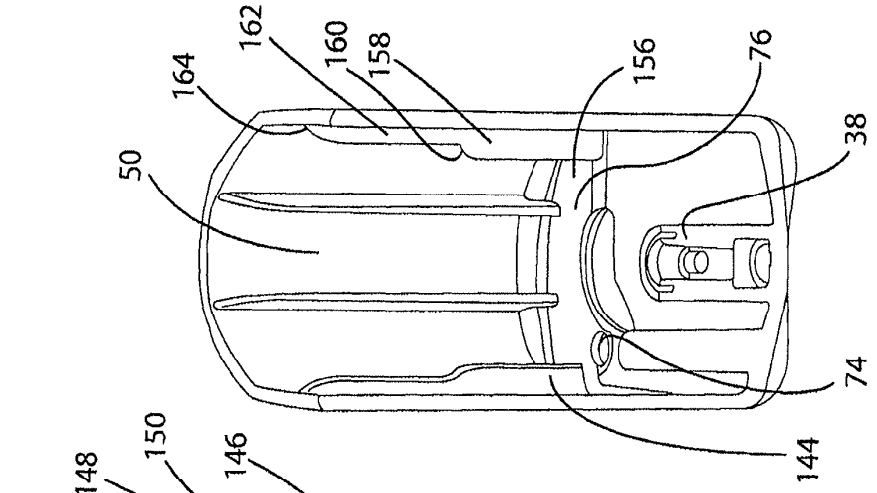


FIG. 7C

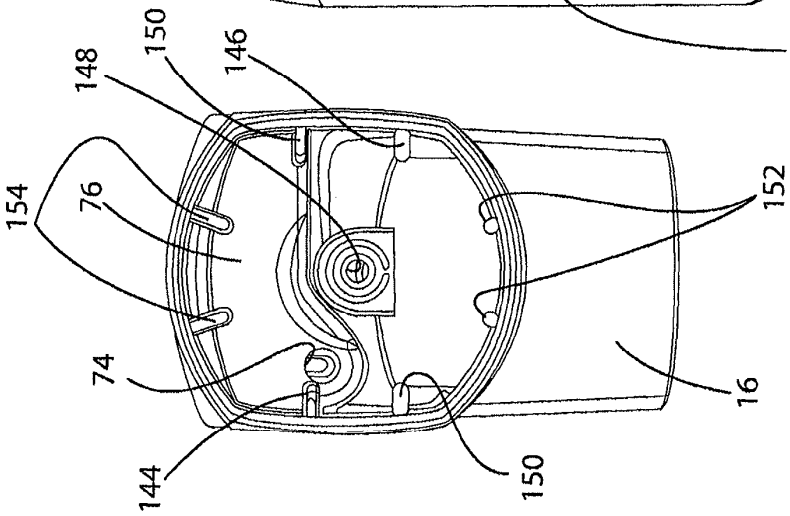


FIG. 7D

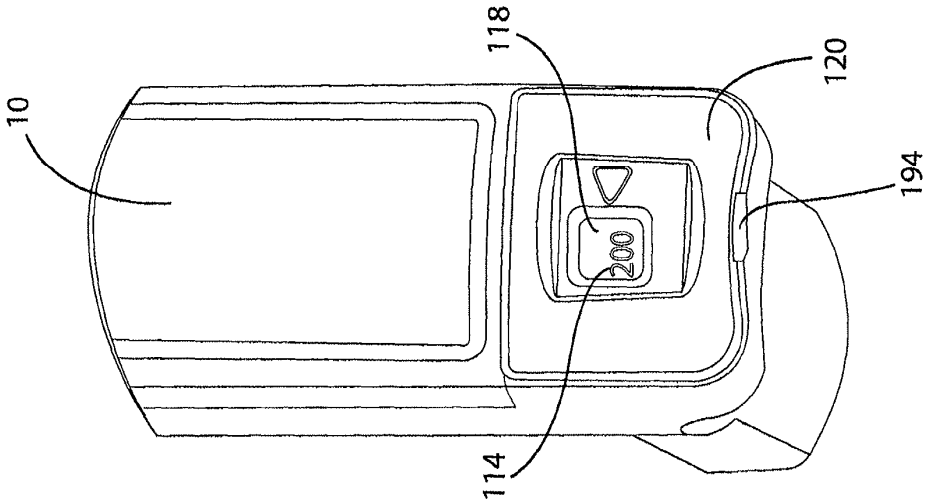


FIG. 8D

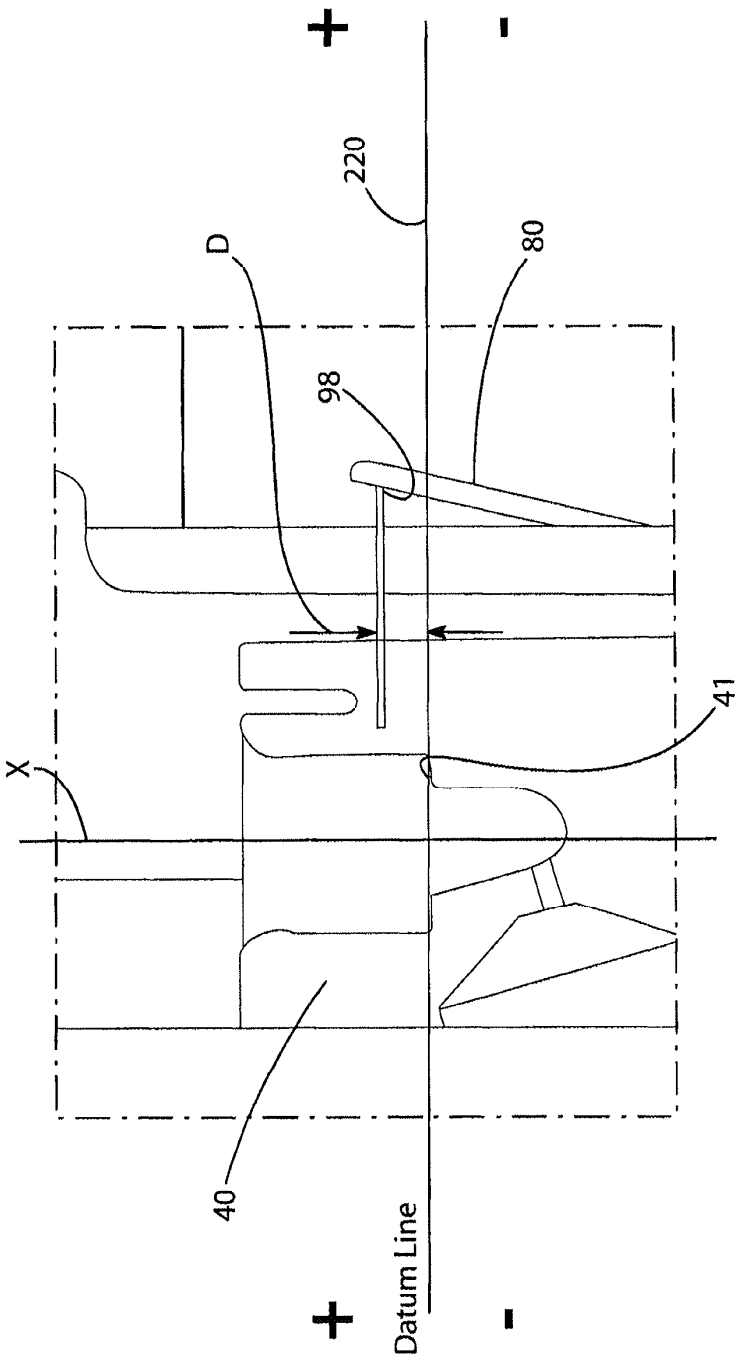


FIG. 9

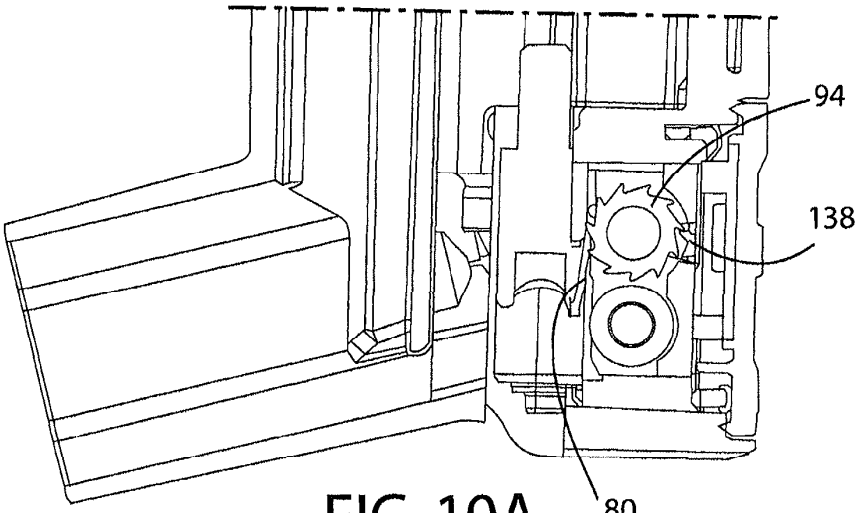


FIG. 10A

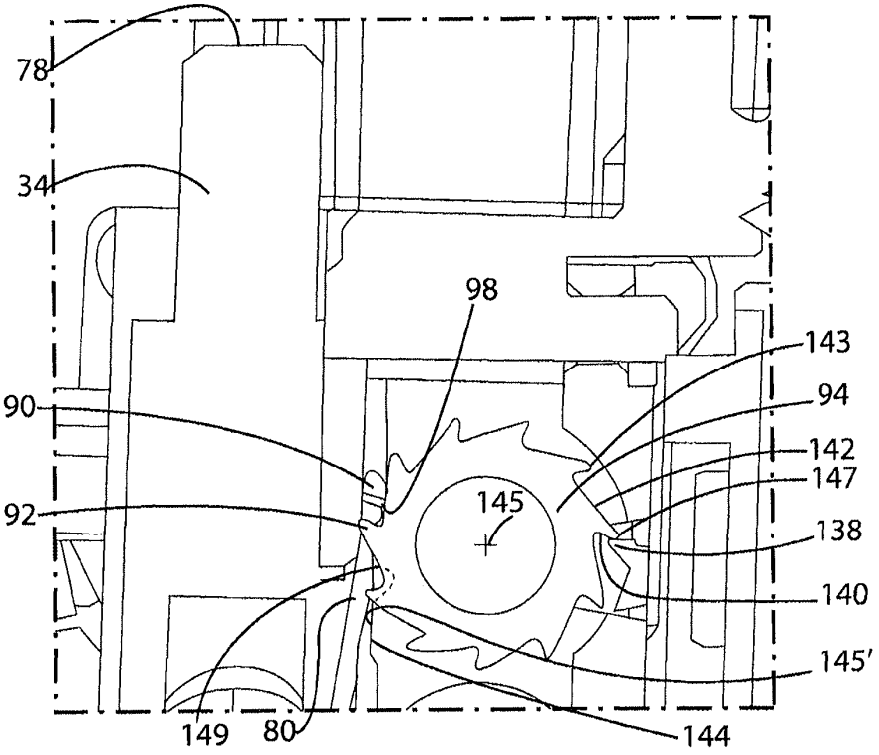


FIG. 10B

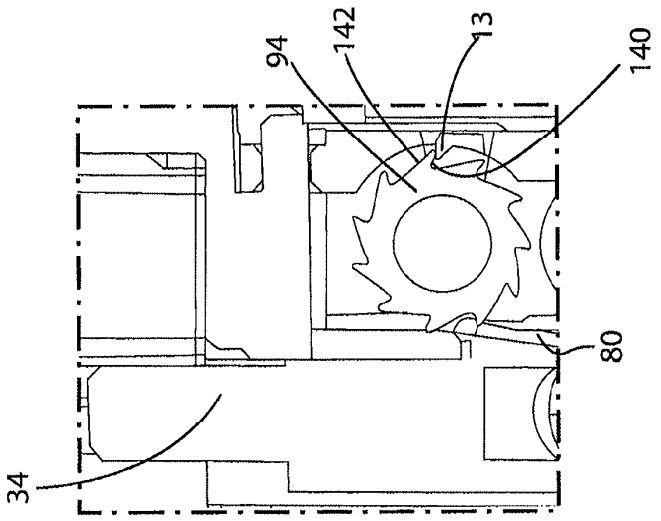


FIG. 10E

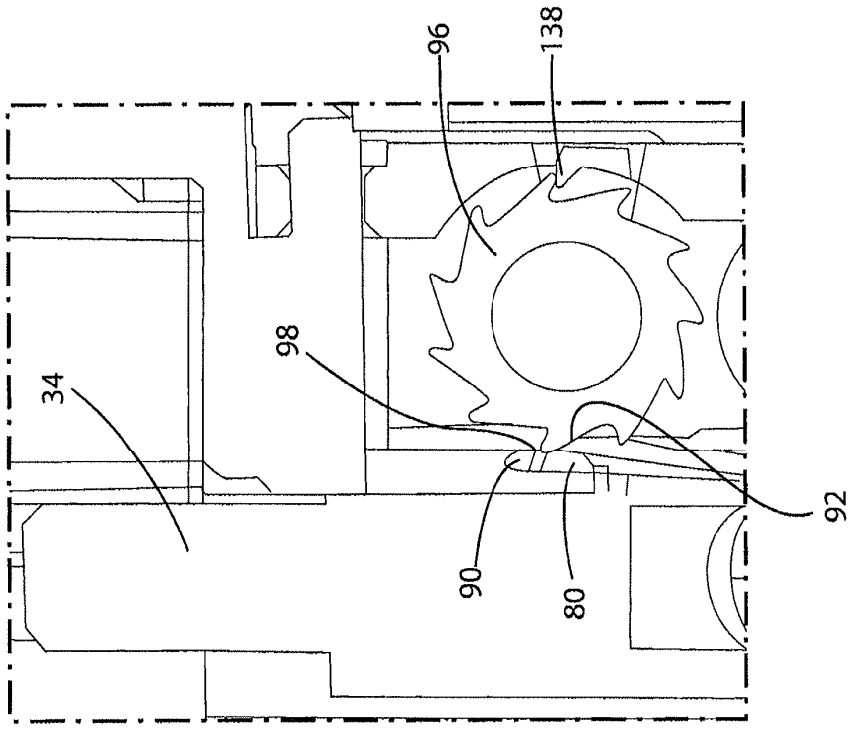


FIG. 10C

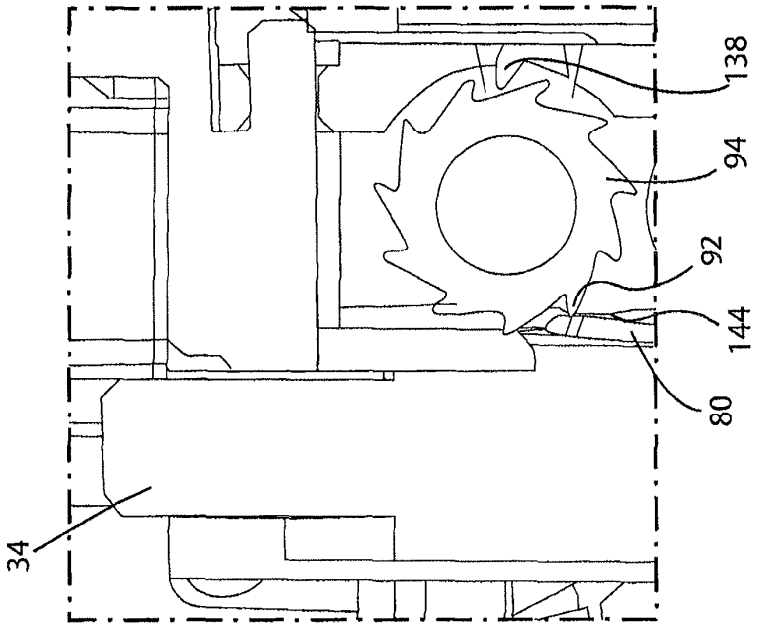


FIG. 10F

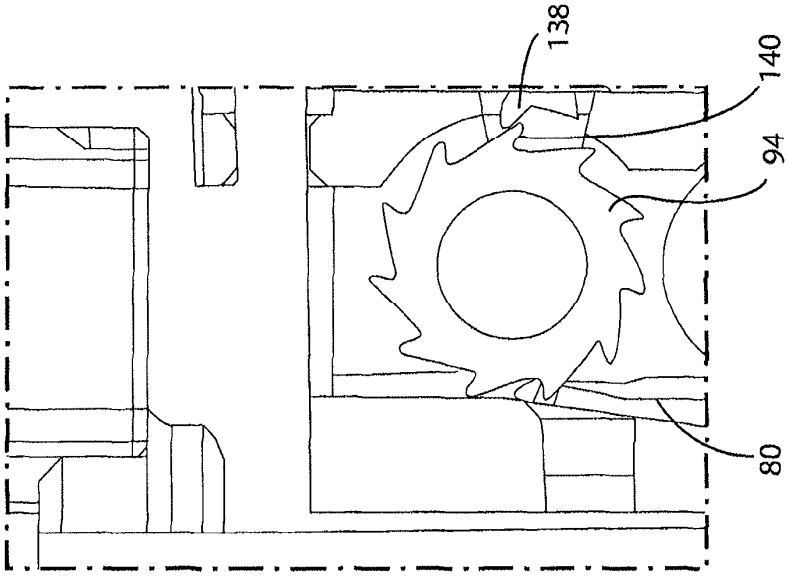


FIG. 10D

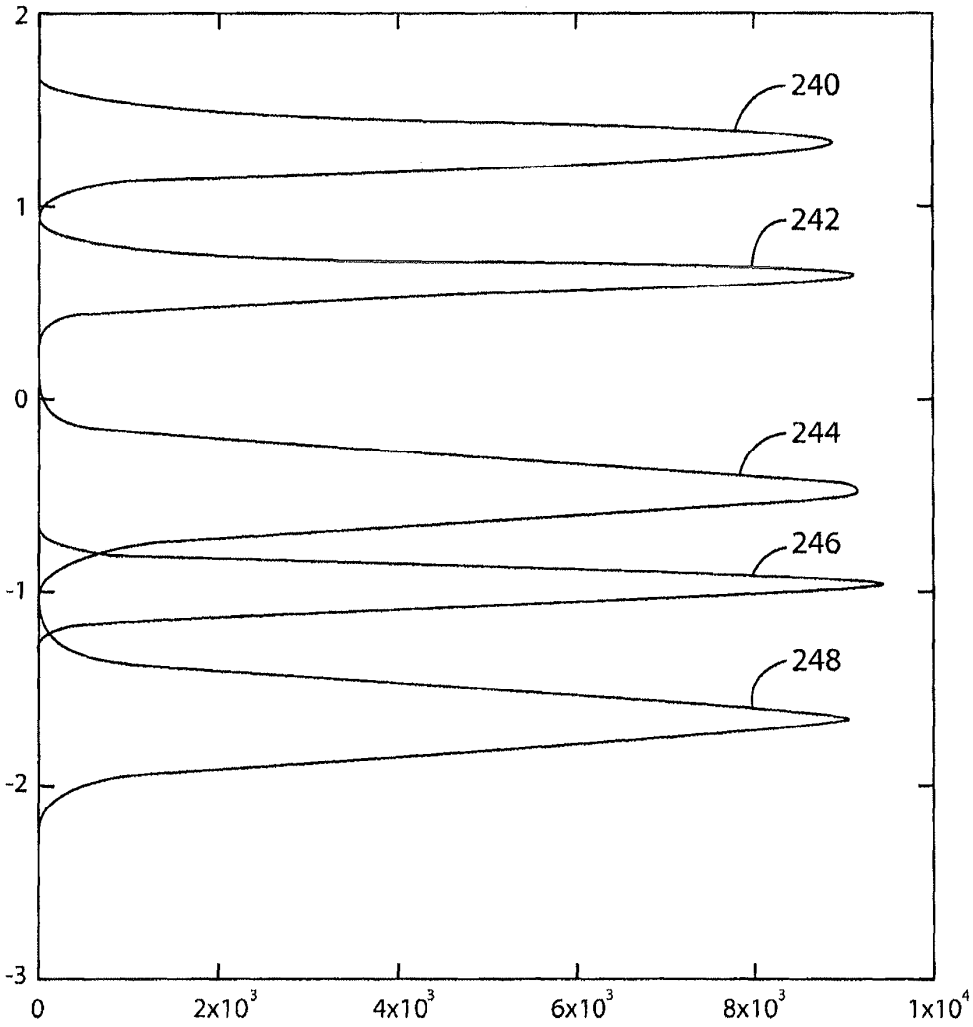

2
1
0
-1
-2
-3
240
242
244
246
248
0
2x10^3
4x10^3
6x10^3
8x10^3
1x10^4

FIG. 11

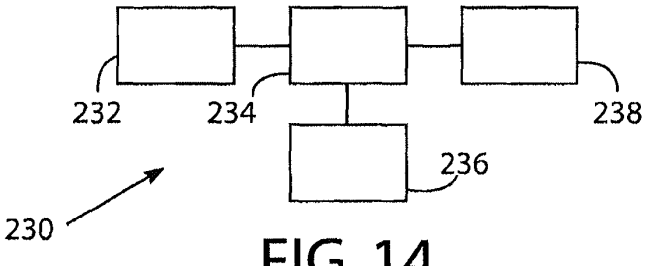

232
234
238
236
230

FIG. 14

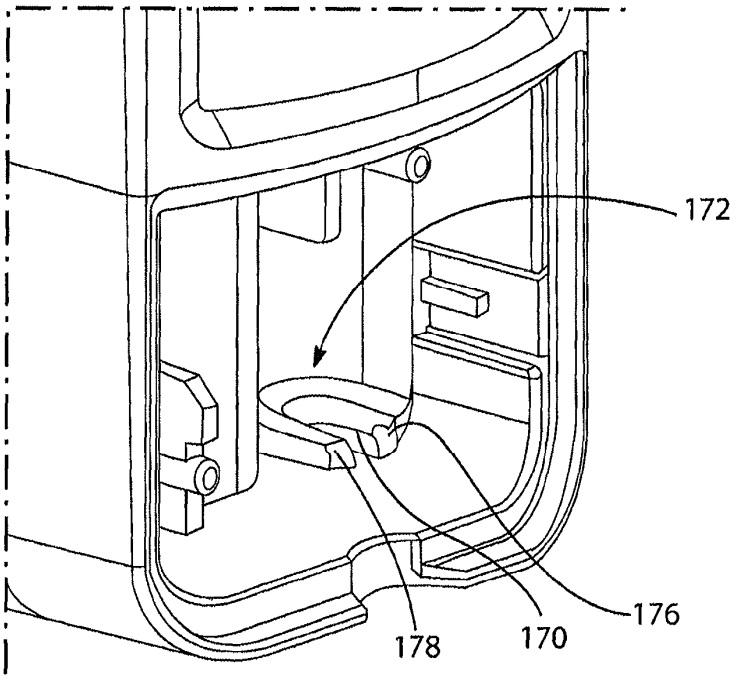


FIG. 12

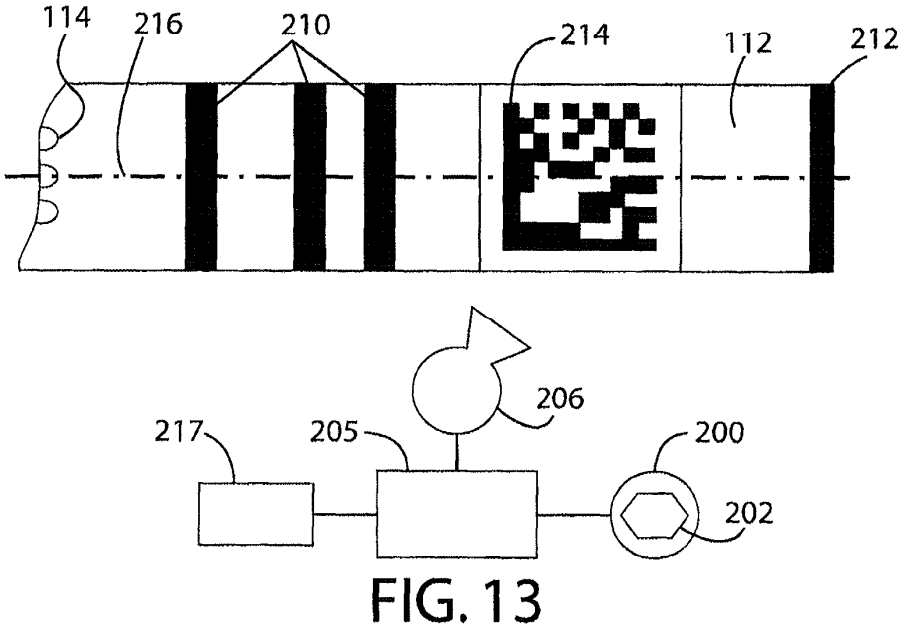


FIG. 13

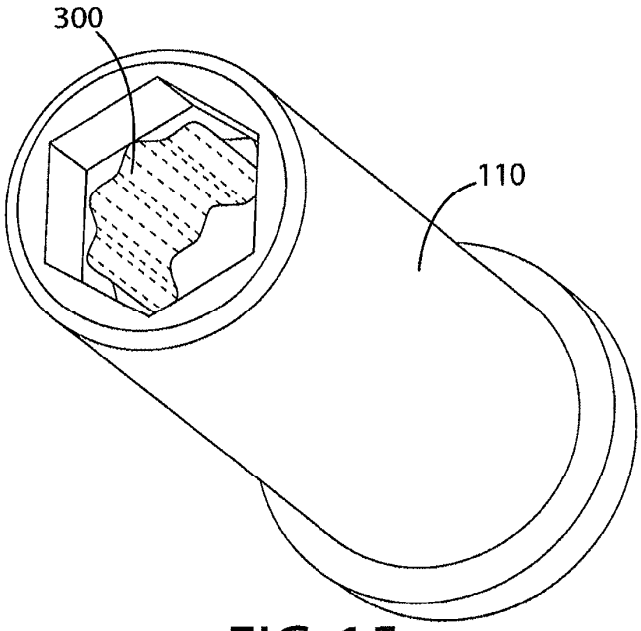


FIG. 15

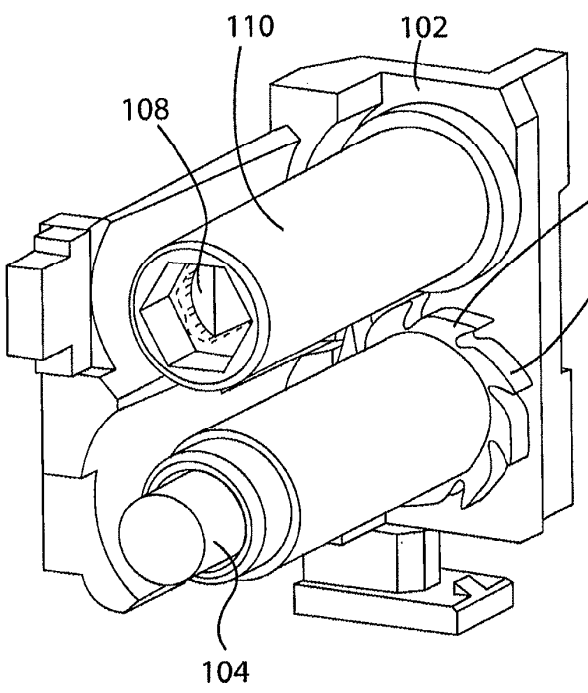


FIG. 20

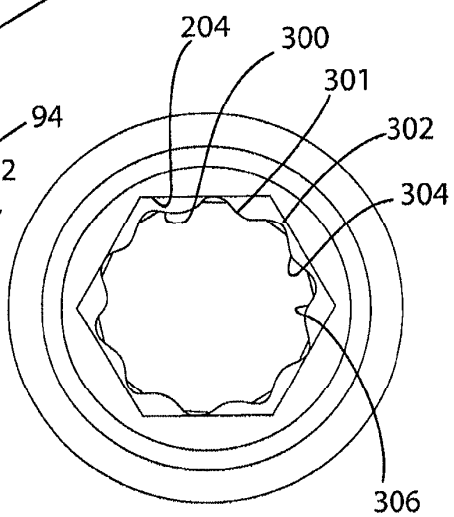


FIG. 16

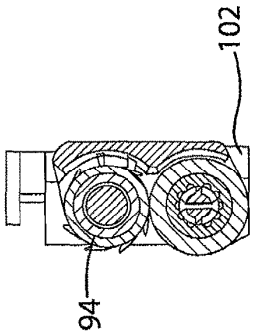


FIG. 19A

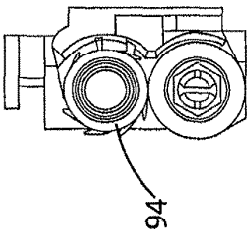


FIG. 19B

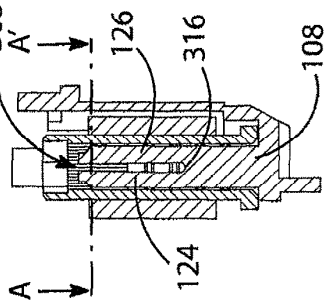


FIG. 19C

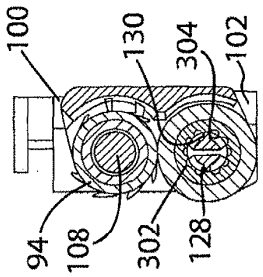


FIG. 18A

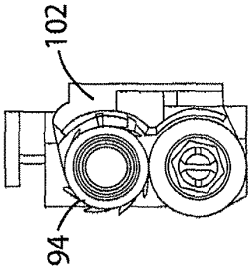


FIG. 18B

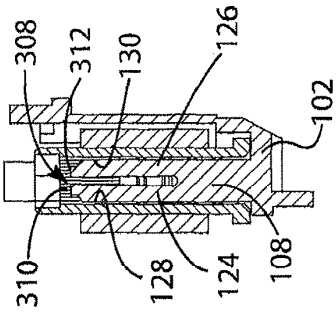


FIG. 18C

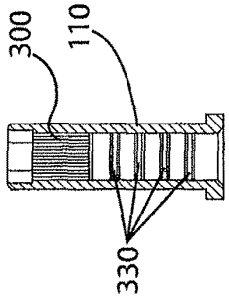


FIG. 17

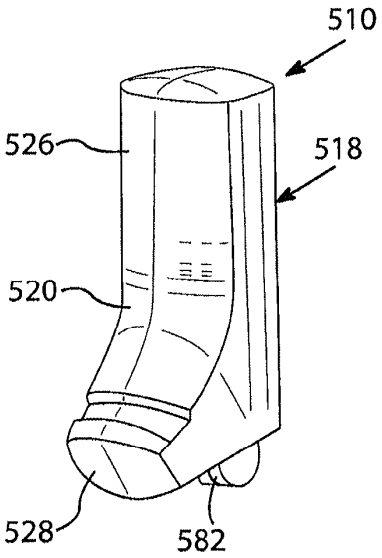

510
526
518
520
528
582

FIG. 21

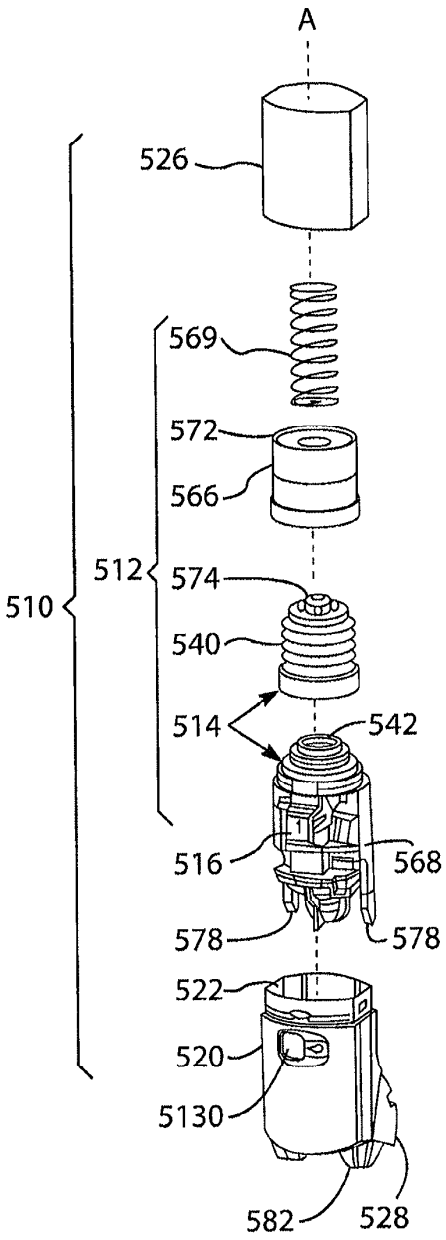

A
526
569
572
566
512
574
510
540
514
542
516
568
578
578
522
520
5130
582
528

FIG. 22

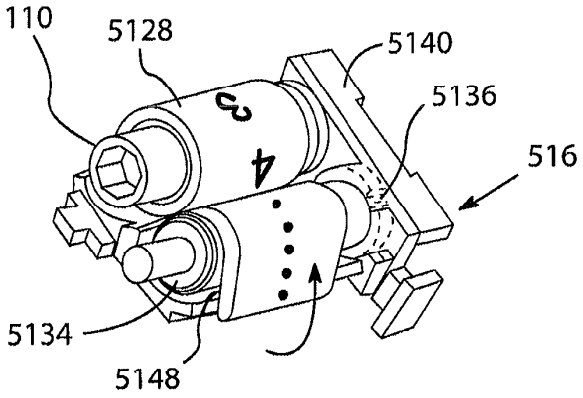

110
5128
5140
5136
516
5134
5148

FIG. 23

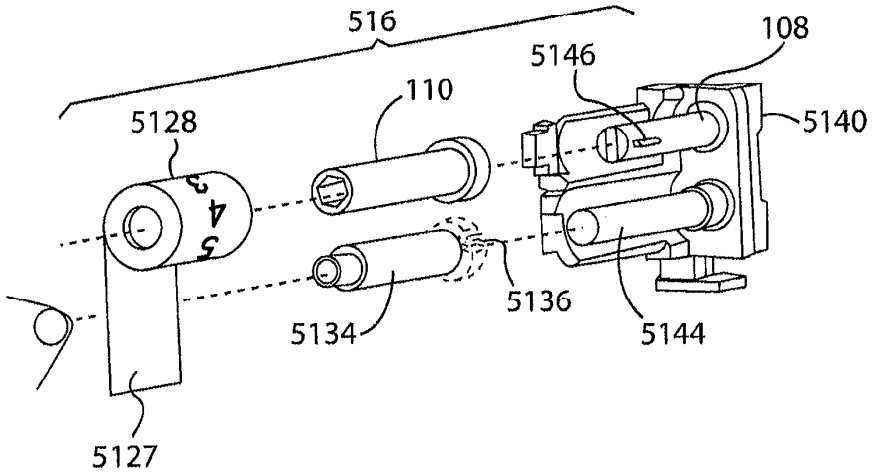

516
108
5146
110
5128
5140
5136
5134
5144
5127

FIG. 24

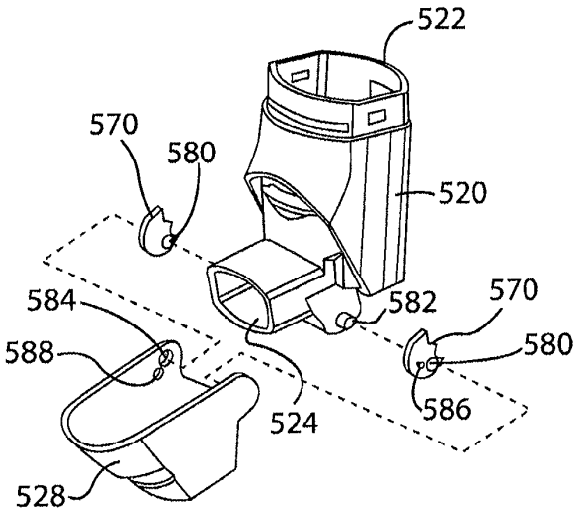


FIG. 25

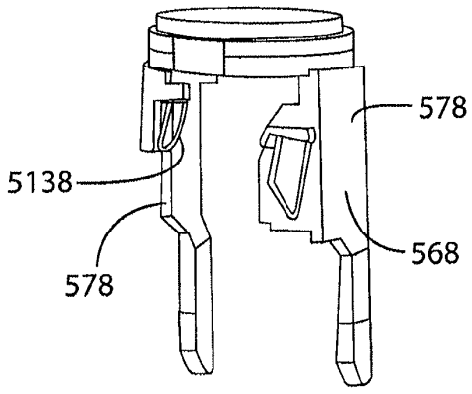


FIG. 26

DOSE COUNTER FOR INHALER HAVING AN ANTI-REVERSE ROTATION ACTUATOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation patent application of U.S. patent application Ser. No. 15/804,735 filed Nov. 6, 2017, which is a continuation of U.S. patent application Ser. No. 15/269,249, filed Sep. 19, 2016, now U.S. Pat. No. 9,808,587, which is a continuation of U.S. patent application Ser. No. 14/103,324, filed Dec. 11, 2013, now U.S. Pat. No. 9,463,289, which is a divisional patent application of U.S. patent application Ser. No. 13/110,532, filed May 18, 2011, now U.S. Pat. No. 8,978,966, which claims priority to U.S. Patent Application No. 61/345,763, filed May 18, 2010, and U.S. Patent Application No. 61/417,659, filed Nov. 29, 2010, each of which is incorporated herein by reference in its entirety for any and all purposes.

FIELD OF THE INVENTION

The present invention relates to dose counters for inhalers, inhalers and methods of assembly thereof. The invention is particularly applicable to metered dose inhalers including dry power medicament inhalers, breath actuated inhalers and manually operated metered dose medicament inhalers.

BACKGROUND OF THE INVENTION

Metered dose inhalers can comprise a medicament-containing pressurised canister containing a mixture of active drug and propellant. Such canisters are usually formed from a deep-dawn aluminium cup having a crimped lid which carries a metering valve assembly. The metering valve assembly is provided with a protruding valve stem which, in use is inserted as a push fit into a stem block in an actuator body of an inhaler having a drug delivery outlet. In order to actuate a manually operable inhaler, the user applies by hand a compressive force to a closed end of the canister and the internal components of the metering valve assembly are spring loaded so that a compressive force of approximately 15 to 30N is required to activate the device in some typical circumstances.

In response to this compressive force the canister moves axially with respect to the valve stem and the axial movement is sufficient to actuate the metering valve and cause a metered quantity of the drug and the propellant to be expelled through the valve stem. This is then released into a mouthpiece of the inhaler via a nozzle in the stem block, such that a user inhaling through the outlet of the inhaler will receive a dose of the drug.

A drawback of self-administration from an inhaler is that it is difficult to determine how much active drug and/or propellant are left in the inhaler, if any, especially of the active drug and this is potentially hazardous for the user since dosing becomes unreliable and backup devices not always available.

Inhalers incorporating dose counters have therefore become known.

WO 98/028033 discloses an inhaler having a ratchet mechanism for driving a tape drive dose counter. A shaft onto which tape is wound has a friction clutch or spring for restraining the shaft against reverse rotation.

EP-A-1486227 discloses an inhaler for dry powered medicament having a ratchet mechanism for a tape dose counter which is operated when a mouthpiece of the inhaler

is closed. Due to the way in which the mouthpiece is opened and closed, and actuation pawl of the device which is mounted on a yoke, travels a known long stroke of consistent length as the mouthpiece is opened and closed.

WO 2008/119552 discloses a metered-dose inhaler which is suitable for breath-operated applications and operates with a known and constant canister stroke length of 3.04 mm+/−0.255 mm. A stock bobbin of the counter, from which a tape is unwound, rotates on a shaft having a split pin intended to hold the stock bobbin taut. However, some dose counters do not keep a particularly reliable count, such as if they are dropped onto a hard surface.

More recently, it has become desirable to improve dose counters further and, in particular, it is felt that it would be useful to provide extremely accurate dose counters for manually-operated canister-type metered dose inhalers. Unfortunately, in these inhalers, it has been found in the course of making the present invention that the stroke length of the canister is to a very large extent controlled on each dose operation by the user, and by hand. Therefore, the stroke length is highly variable and it is found to be extremely difficult to provide a highly reliable dose counter for these applications. The dose counter must not count a dose when the canister has not fired since this might wrongly indicate to the user that a dose has been applied and if done repeatedly the user would throw away the canister or whole device before it is really time to change the device due to the active drug and propellant reaching a set minimum. Additionally, the canister must not fire without the dose counter counting because the user may then apply another dose thinking that the canister has not fired, and if this is done repeatedly the active drug and/or propellant may run out while the user thinks the device is still suitable for use according to the counter. It has also been found to be fairly difficult to assembly some known inhaler devices and the dose counters therefor. Additionally, it is felt desirable to improve upon inhalers by making them easily usable after they have been washed with water.

The present invention aims to alleviate at least to a certain extent one or more of the problems of the prior art.

SUMMARY OF THE INVENTION

According to a first aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a counter display arranged to indicate dosage information, a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

The regulator is advantageous in that it helps prevent unwanted motion of the counter display if the counter is dropped.

According to a further aspect of the present invention, the regulator provides a resistance force of greater than 0.1 N against movement of the counter display. According to still a further aspect of the present invention, the resistance force is greater than 0.3 N. According to yet a further aspect of the present invention, the resistance force is from 0.3 to 0.4 N.

Preferably, the counter comprises a tape.

Preferably, the tape has dose counter indicia displayed thereon. The first station may comprise a region of the dose counter where tape is held which is located before a display location, such as a display window, for the counter indicia.

The first station may comprise a first shaft, the tape being arranged on the first shaft and to unwind therefrom upon movement of the counter display.

The first shaft may be mounted for rotation relative to a substantially rotationally fixed element of the dose counter.

The regulator may comprise at least one projection which is arranged on one of the first shaft and the substantially rotationally fixed element and to engage incrementally with one or more formations on the other of the first shaft and the substantially rotationally fixed element.

At least two said projections may be provided. Exactly two said projections maybe provided.

Each projection may comprise a radiused surface.

The at least one projection may be located on the substantially fixed element which may comprise a fixed shaft which is fixed to a main body of the dose counter, the first shaft being rotationally mounted to the fixed shaft.

Preferably, the fixed shaft has at least two resiliently flexible legs (or forks). Each leg may have at least one said projection formed in an outwardly facing direction thereon, said one or more formations being formed on an inwardly facing engagement surface of the first shaft, said at least one projection being arranged to resiliently engage said one or more formations. Preferably, a series of said formations are provided. An even number of said formations may be provided. Eight to twelve of said formations may be provided. In one embodiment, ten said formations are provided.

Each said formation may comprise a concavity formed on an engagement surface. Each concavity may comprise a radiused surface wall portion which preferably merges on at least one side thereof into a flat wall portion surface. The engagement surface may include a series of said concavities, and convex wall portions of the engagement surface may be formed between each adjacent two said concavities, each said convex wall portion comprising a convex radiused wall portion.

Each convex radiused wall portion of each convex wall portion may be connected by said flat wall portion surfaces to each adjacent concavity.

The fixed shaft may comprise a split pin with fork legs and each projection may be located on a said fork leg.

The first shaft may comprise a substantially hollow bobbin.

Said at least one formation may be located on an inner surface of the bobbin. In other embodiments it may be located on an outer surface thereof. Said engagement surface may extend partially along said bobbin, a remainder of the respective inner or outer surface having a generally smooth journal portion along at least a portion thereof.

The drive system may comprise a tooth ratchet wheel arranged to act upon a second shaft which is located at the second station, the second shaft being rotatable to wind the tape onto the second shaft.

The second shaft may be located on a main body of the dose counter spaced from and parallel to the first shaft.

The ratchet wheel may be fixed to the second shaft is arranged to rotate therewith. The ratchet wheel may be secured to an end of the second shaft and aligned coaxially with the second shaft.

The dose counter may include anti-back drive system which is arranged to restrict motion of the second shaft. The anti-back drive system may include a substantially fixed tooth arranged to act upon teeth of the ratchet wheel.

According to a further aspect of the present invention, a dose counter includes an anti-back drive system which is arranged to restrict motion of the second shaft in a tape winding direction.

According to a further aspect of the present invention there is provided a shaft for holding counter tape in a dose counter for an inhaler, the shaft having an engagement surface including incrementally spaced formations located around a periphery thereof, the formations comprising a series of curved concavities and convex portions.

The shaft may comprise a hollow bobbin.

The engagement surface may be a generally cylindrical inwardly directed surface.

The engagement surface may include a flat surface wall portion joining each concavity and convex wall portion.

Each concavity may comprise a radiused wall portion.

Each convex wall portion may comprise a radiused wall portion.

Said concavities may be regularly spaced around a longitudinal axis of the shaft.

Said convex wall portions may be regularly spaced around a longitudinal axis of the shaft.

In some embodiments there may be from eight to twelve said concavities and/or convex wall portions regularly spaced around a longitudinal axis thereof.

One embodiment includes ten said concavities and/or convex wall portions regularly spaced around a longitudinal axis of the shaft.

According to a further aspect of the present invention there is provided a shaft and counter tape assembly for use in a dose counter for an inhaler, the assembly comprising a rotatable shaft and a counter tape which is wound around the shaft and is adapted to unwind therefrom upon inhaler actuation, the shaft having an engagement surface which includes incrementally spaced formations located around a periphery thereof.

According to a further aspect of the present invention there is provided an inhaler for the inhalation of medication and the like, the inhaler including a dose counter as in the first aspect of the present invention.

A preferred construction consists of a manually operated metered dose inhaler including a dose counter chamber including a dose display tape driven by a ratchet wheel which is driven in turn by an actuator pawl actuated by movement of a canister, the tape unwinding from a stock bobbin during use of the inhaler, a rotation regulator being provided for the stock bobbin and comprising a wavelike engagement surface with concavities which engage against control elements in the form of protrusions on resilient forks of a split pin thereby permitting incremental unwinding of the stock bobbin yet resisting excessive rotation if the inhaler is dropped onto a hard surface.

According to another aspect of the present invention there is provided a dose counter for a metered dose inhaler having a body arranged to retain a medicament canister of predetermined configuration for movement of the canister relative thereto; the dose counter comprising: an incremental counting system for counting doses, the incremental counting system having a main body, an actuator arranged to be driven in response to canister motion and to drive an incremental output member in response to canister motion, the actuator and incremental output member being configured to have predetermined canister fire and count configurations in a canister fire sequence, the canister fire configuration being determined by a position of the actuator relative to a datum at which the canister fires medicament and the count configuration being determined by a position of the actuator relative to the datum at which the incremental count system makes an incremental count, wherein the actuator is

arranged to reach a position thereof in the count configuration at or after a position thereof in the canister fire configuration.

This arrangement has been found to be highly advantageous since it provides an extremely accurate dose counter which is suitable for use with manually operated metered dose inhalers. It has been found that dose counters with these features have a failure rate of less than 50 failed counts per million full canister activation depressions. It has been found in the course of making the present invention that highly reliable counting can be achieved with the dose counter counting at or soon after the point at which the canister fires. It has been is covered by the present inventors that momentum and motion involved in firing the canister, and in some embodiments a slight reduction in canister back pressure on the user at the time of canister firing, can very reliably result in additional further motion past the count point.

The actuator and incremental counting system may be arranged such that the actuator is displaced less than 1 mm, typically 0.25 to 0.75 mm, more preferably about 0.4 to 0.6 mm, relative to the body between its location in the count and fire configurations, about 0.48 mm being preferred. The canister, which can move substantially in line with the actuator, can reliably move this additional distance so as to achieve very reliable counting.

The incremental count system may comprise a ratchet mechanism and the incremental output member may comprise a ratchet wheel having a plurality of circumferentially spaced teeth arranged to engage the actuator.

The actuator may comprise an actuator pawl arranged to engage on teeth of the ratchet wheel. The actuator pawl may be arranged to be connected to or integral with an actuator pin arranged to engage and be depressed by a medicament canister bottom flange. The actuator pawl may be generally U-shaped having two parallel arms arranged to pull on a central pawl member arranged substantially perpendicular thereto. This provides a very reliable actuator pawl which can reliably pull on the teeth of the ratchet wheel.

The incremental count system may include a tape counter having tape with incremental dose indicia located thereon, the tape being positioned on a tape stock bobbin and being arranged to unwind therefrom.

The actuator and incremental output member may be arranged to provide a start configuration at which the actuator is spaced from the ratchet output member, a reset configuration at which the actuator is brought into engagement with the incremental output member during a canister fire sequence, and an end configuration at which the actuator disengages from the ratchet output during a canister fire sequence.

The actuator may be arranged to be located about 1.5 to 2.0 mm, from its location in the fire configuration, when in the start configuration, about 1.80 mm being preferred.

The actuator may be arranged to be located about 1.0 to 1.2 mm, from its location in the fire configuration, when in the reset configuration, about 1.11 mm being preferred.

The actuator may be arranged to be located about 1.1 to 1.3 mm, from its location in the fire configuration, when in the end configuration, about 1.18 mm being preferred.

These arrangements provide extremely reliable dose counting, especially with manually operated canister type metered dose inhalers.

The main body may include a formation for forcing the actuator to disengage from the incremental output member when the actuator is moved past the end configuration. The formation may comprise a bumped up portion of an otherwise generally straight surface against which the actuator engages and along which it is arranged to slide during a canister firing sequence.

The dose counter may include a counter pawl, the counter pawl having a tooth arranged to engage the incremental output member, the tooth and incremental output member being arranged to permit one way only incremental relative motion therebetween. When the incremental output member comprises a ratchet wheel, the tooth can therefore serve as an anti-back drive tooth for the ratchet wheel, thereby permitting only one way motion or rotation thereof.

The counter pawl may be substantially fixedly mounted on the main body of the incremental count system and the counter pawl may be arranged to be capable of repeatedly engaging equi-spaced teeth of the incremental output member in anti-back drive interlock configurations as the counter is operated. The counter pawl may be positioned so that the incremental output member is halfway, or substantially halfway moved from one anti-back drive interlock configuration to the next when the actuator and incremental output member are in the end configuration thereof. This is highly advantageous in that it minimises the risk of double counting or non-counting by the dose counter.

According to a further aspect of the invention there is provided an inhaler comprising a main body arranged to retain a medicament canister of predetermined configuration and a dose counter mounted in the main body.

The inhaler main body may include a canister receiving portion and a separate counter chamber, the dose counter being located within the main body thereof, the incremental output member and actuator thereof inside the counter chamber, the main body of the inhaler having wall surfaces separating the canister-receiving portion and the counter chamber, the wall surfaces being provided with a communication aperture, an actuation member extending through the communication aperture to transmit canister motion to the actuator.

According to a further aspect of the present invention there is a provided an inhaler for metered dose inhalation, the inhaler comprising a main body having a canister housing arranged to retain a medicament canister for motion therein, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of a medicament canister, wherein the canister housing has an inner wall, and a first inner wall canister support formation located directly adjacent the actuation member.

This is highly advantageous in that the first inner wall canister support formation can prevent a canister from rocking too much relative to the main body of the inhaler. Since the canister may operate the actuation member of the dose counter, this substantially improves dose counting and avoids counter errors.

The canister housing may have a longitudinal axis which passes through a central outlet port thereof, the central outlet port being arranged to mate with an outer canister fire stem of a medicament canister, the inner wall canister support formation, the actuation member and the outlet port lying in a common plane coincident with the longitudinal axis. Accordingly, this construction may prevent the canister from rocking towards the position of the dose counter actuation member, thereby minimising errors in counting.

The canister housing may have a further inner canister wall support formation located on the inner wall opposite, or substantially opposite, the actuation member. Accordingly, the canister may be supported against rocking motion away from the actuator member so as to minimise count errors.

The canister housing may be generally straight and tubular and may have an arrangement in which each said inner wall support formation comprises a rail extending longitudinally along the inner wall.

Each said rail may be stepped, in that it may have a first portion located towards a medicine outlet end or stem block of the canister housing which extends inwardly a first distance from a main surface of the inner wall and a second portion located toward an opposite end of the canister chamber which extends inwardly a second, smaller distance from the main surface of the inner wall. This may therefore enable easy insertion of a canister into the canister housing such that a canister can be lined up gradually in step wise function as it is inserted into the canister housing.

The inhaler may include additional canister support rails which are spaced around an inner periphery of the inner wall of the canister housing and which extend longitudinally therealong.

At least one of the additional rails may extend a constant distance inwardly from the main surface of the inner wall.

At least one of the additional rails may be formed with a similar configuration to the first inner wall canister support formation.

The dose counter may, apart from said at least a portion of the actuation member, be located in a counter chamber separate from the canister housing, the actuation member comprising a pin extending through an aperture in a wall which separates the counter chamber and the canister housing.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicaments having: a body for retaining a medicament store; the body including a dose counter, the dose counter having a moveable actuator and a return spring for the actuator, the return spring having a generally cylindrical and annular end; the body having a support formation therein for supporting said end of the return spring, the support formation comprising a shelf onto which said end is engageable and a recess below the shelf.

This shelf and recess arrangement is highly advantageous since it allows a tool (such as manual or mechanical tweezers) to be used to place the return spring of the actuator onto the shelf with the tool then being withdrawn at least partially via the recess.

The shelf may be U-shaped.

The support formation may include a U-shaped upstanding wall extending around the U-shaped shelf, the shelf and upstanding wall thereby forming a step and riser of a stepped arrangement.

The recess below the shelf my also be U-shaped.

At least one chamfered surface may be provided at an entrance to the shelf. This may assist in inserting the actuator and return spring into position.

A further aspect of the invention provides a method of assembly of an inhaler which includes the step of locating said end of said spring on the shelf with an assembly tool and then withdrawing the assembly tool at least partly via the recess. This assembly method is highly advantageous compared to prior art methods in which spring insertion has been difficult and in which withdrawal of the tool has sometimes accidentally withdrawn the spring again.

The cylindrical and annular end of the spring may be movable in a direction transverse to its cylindrical extent into the shelf while being located thereon.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament, the inhaler having a body for retaining a medicament store; and a dose counter, the dose counter having a moveable actuator and a chassis mounted on the body; the chassis being heat staked in position on the body. This is be highly advantageous in that the chassis can be very accurately positioned and held firmly in place, thereby further improving counting accuracy compared to prior art arrangements in which some movement of the chassis relative to the body may be tolerated in snap-fit connections.

The chassis may have at least one of a pin or aperture heat staked to a respective aperture or pin of the body.

The chassis may have a ratchet counter output member mounted thereon.

The ratchet counter output member may comprise a ratchet wheel arranged to reel in incrementally a dose meter tape having a dosage indicia located thereon.

According to a further aspect of the present invention there is provided a method of assembling an inhaler including the step of heat staking the chassis onto the body. The step of heat staking is highly advantageous in fixedly positioning the chassis onto the body in order to achieve highly accurate dose counting in the assembled inhaler.

The method of assembly may include mounting a spring-returned ratchet actuator in the body before heat staking the chassis in place. The method of assembly may include pre-assembling the chassis with a dose meter tape prior to the step of heat staking the chassis in place. The method of assembly may include attaching a dose meter cover onto the body after the heat staking step. The cover may be welded onto the body or may in some embodiments be glued or otherwise attached in place.

According to a further aspect of the present invention there is provided an inhaler for inhaling medicament and having a body, the body have a main part thereof for retaining a medicament store; and a dose counter, the dose counter being located in a dose counter chamber of the body which is separated from the main part of the body, the dose counter chamber of the body having a dosage display and being perforated so as to permit the evaporation of water or aqueous matter in the dose counter chamber into the atmosphere.

This is high advantageous since it enables the inhaler to be thoroughly washed and the dose counting chamber can thereafter dry out fully.

The display may comprise a mechanical counter display inside the dose counter chamber and a window for viewing the mechanical counter display. The mechanical counter display may comprise a tape. The perforated dose counter chamber may therefore enable reliable washing of the inhaler, if desired by the user, and may therefore dry out without the display window misting up.

The dose counter chamber may be perforated by a drain hole formed through an outer hole of the body. The drain hole may be located at a bottom portion of the body of the inhaler, thereby enabling full draining of the inhaler to be encouraged after washing when the inhaler is brought into an upright position.

According to a further aspect of the present invention there is provided a dose counter for an inhaler, the dose counter having a display tape arranged to be incrementally driven from a tape stock bobbin onto an incremental tape take-up drive shaft, the bobbin having an internal bore supported by and for rotation about a support shaft, at least one of the bore and support shaft having a protrusion which is resiliently biased into frictional engagement with the other of the bore and support shaft with longitudinally extending mutual frictional interaction. This arrangement may provide good friction for the bobbin, thereby improving tape counter

display accuracy and preventing the bobbin from unwinding undesirably for example if the inhaler is accidentally dropped.

The support shaft may be forked and resilient for resiliently biasing the support shaft and bore into frictional engagement.

The support shaft may have two forks, or more in some cases, each having a radially extending protrusion having a friction edge extending therealong parallel to a longitudinal axis of the support shaft for frictionally engaging the bore of the support shaft with longitudinally extending frictional interaction therebetween.

The bore may be a smooth circularly cylindrical or substantially cylindrical bore.

Each of the above inhalers in accordance with aspects of the present invention may have a medicament canister mounted thereto.

The canister may comprise a pressurised metered dose canister having a reciprocally movable stem extending therefrom and movable into a main canister portion thereof for releasing a metered dose of medicament under pressure, for example by operating a metered dose valve inside the canister body. The canister may be operable by pressing by hand on the main canister body.

In cases in which one or more support rails or inner wall support formations are provided, the canister may at all times when within the canister chamber have a clearance of about 0.25 to 0.35 mm from the first inner wall support formation. The clearance may be almost exactly 0.3 mm. This clearance which may apply to the canister body itself or to the canister once a label has been applied, is enough to allow smooth motion of the canister in the inhaler while at the same time preventing substantial rocking of the canister which could result in inaccurate counting by a dose counter of the inhaler, especially when lower face of the canister is arranged to engage an actuator member of the dose counter for counting purposes.

According to a further aspect of the invention, a method of assembling a dose counter for an inhaler comprises the steps of providing a tape with dosing indicia thereon; providing tape positioning indicia on the tape; and stowing the tape while monitoring for the tape positioning indicia with a sensor. The method advantageously permits efficient and accurate stowing of the tape, e.g. by winding.

The dosing indicia may be provided as numbers, the tape positioning indicia may be provided as one or more lines across the tape. The stowing step comprises winding the tape onto a bobbin or shaft, and, optionally, stopping winding when the positioning indicia are in a predetermined position. The tape may be provided with pixelated indicia at a position spaced along the tape from the positioning indicia.

The tape may also be provided with a priming dot.

According to a further aspect of the invention, a tape system for a dose counter for an inhaler has a main elongate tape structure, and dosing indicia and tape positioning indicia located on the tape structure. The tape positioning indicia may comprise at least one line extending across the tape structure. The tape system may comprise pixelated indicia located on the tape structure and spaced from the positioning indicia. The tape system may comprise a priming dot located on the tape structure. The positioning indicia may be located between the timing dot and the pixelated indicia. The main elongate tape structure may have at least one end thereof wound on a bobbin or shaft.

A further aspect of the invention provides a method of designing an incremental dose counter for an inhaler comprising the steps of calculating nominal canister fire and dose counter positions for a dose counter actuator of the inhaler; calculating a failure/success rate for dose counters built to tolerance levels for counting each fire of inhalers in which the dose counter actuators may be applied; and selecting a tolerance level to result in said failure/success rate to be at or below/above a predetermined value. This is highly advantageous in that it allows an efficient and accurate prediction of the reliability of a series of inhaler counters made in accordance with the design.

The method of designing may include selecting the failure/success rate as a failure rate of no more than one in 50 million. The method of designing may include setting an average count position for dose counters built to the tolerances to be at or after an average fire position thereof during canister firing motion. The method of designing may include setting the average count position to be about 0.4 to 0.6 mm after the average fire position, such as about 0.48 mm after. The method of designing may include setting tolerances for the standard deviation of the fire position in dose counters built to the tolerances to be about 0.12 to 0.16 mm, such as about 0.141 mm. The method of designing may include setting tolerances for the standard deviation of the count positions in dose counters built to the tolerances to be about 0.07 to 0.09 mm, such as about 0.08 mm. A further aspect of the invention provides a computer implemented method of designing an incremental dose counter for an inhaler which includes the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing in a production run a series of incremental dose counters for inhalers which comprises manufacturing the series of dose counters in accordance with the aforementioned method of designing.

A further aspect of the invention provides a method of manufacturing a series of incremental dose counters for inhalers, which comprises manufacturing the dose counters with nominal canister fire and dose count positions of a dose counter actuator relative to a dose counter chassis (or inhaler main body), and which includes building the dose counters with the average dose count position in the series being, in canister fire process, at or after the average canister fire position in the series.

According to a further aspect of the invention, the method provides fitting each dose counter in the series of incremental dose counters to a corresponding main body of an inhaler.

These aspects advantageously provide for the production run of a series of inhalers and dose counters which count reliably in operation.

According to a further aspect of the invention, an incremental dose counter for a metered dose inhaler has a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction. This advantageously enables an inhaler dose counter to keep a reliable count of remaining doses even if dropped or otherwise jolted.

The output member may comprise a ratchet wheel. The actuator may comprise a pawl and in which the ratchet wheel and pawl are arranged to permit only one-way ratcheting motion of the wheel relative to the pawl. The dose counter may include an anti-back drive member fixed to the main body. In a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the anti-back drive member and the pawl is spaced from an adjacent back

surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and wheel.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention may be carried out in various ways and preferred embodiment of a dose counter, inhaler and methods of assembly, design and manufacture will now be described with reference to the accompanying drawings in which:

FIG. **1** is an isometric view of a main body of an embodiment of an inhaler related to the invention together with a mouthpiece cap therefor;

FIG. **2** is a top plan view of the components as shown in FIG. **1**;

FIG. **3**A is a section on the plane **3**A-**3**A in FIG. **2**;

FIG. **3**B is a view corresponding to FIG. **3**A but with a dose counter fitted to the main body of the inhaler;

FIG. **4**A is an exploded view of the inhaler main body, mouthpiece cap, dose counter and a dose counter window;

FIG. **4**B is a view in the direction **4**B in FIG. **4**C of a spring retainer of the dose counter;

FIG. **4**C is a top view of the spring retainer of FIG. **4**B;

FIG. **5** is a bottom view of the assembled inhaler main body, mouthpiece cap, dose counter and dose counter window;

FIGS. **6**A, **6**B, **6**C, **6**D, **6**E, **6**F, **6**G and **6**H are various views of dose counter components of the inhaler;

FIGS. **7**A and **7**B are sectional views showing canister clearance inside the main body of the inhaler;

FIG. **7**C is a further sectional view similar to that of FIG. **7**B but with the canister removed;

FIG. **7**D is a top plan view of the inhaler main body;

FIGS. **8**A, **8**B, **8**C and **8**D show the inhaler main body and dose counter components during assembly thereof;

FIG. **9** shows a sectional side view of a datum line for an actuator pawl of the dose counter;

FIGS. **10**A, **10**B, **10**C, **10**D, **10**E and **10**F show various side views of positions and configurations of the actuator pawl, a ratchet wheel, and a count pawl;

FIG. **11** shows distributions for tolerances of start, reset, fire, count and end positions for the actuator of the dose counter;

FIG. **12** is an enlarged version of part of FIG. **4**A;

FIG. **13** shows an end portion of a tape of the dose counter;

FIG. **14** shows a computer system for designing the dose counter;

FIG. **15** is an isometric view of a stock bobbin modified in accordance with the present invention for use in the dose counter of the inhaler of FIGS. **1** to **14**;

FIG. **16** shows an end view of the stock bobbin of FIG. **15**;

FIG. **17** is a section through a longitudinal axis of the stock bobbin of FIGS. **15** and **16**;

FIGS. **18**A, **18**B and **18**C are views of the stock bobbin of FIGS. **15** to **17** mounted in the dose counter chassis of FIGS. **1** to **14**, with the control elements of the forks of the second shaft (or split pin) having a profile slightly different to that in FIG. **6**F, with the forks in a compressed configuration;

FIGS. **19**A, **19**B and **19**C are views equivalent to FIGS. **18**A to **18**C but with the forks in a more expanded configuration due to a different rotational position of the stock bobbin;

FIG. **20** is an isometric view of the chassis assembled and including the stock bobbin of FIGS. **15** to **17** but excluding the tape for reasons of clarity;

FIG. **21** is a view of a preferred embodiment of a dry powder inhaler in accordance with the present invention;

FIG. **22** is an exploded view of the inhaler of FIG. **21**;

FIG. **23** is a view of a dose counter of the inhaler of FIG. **21**;

FIG. **24** is an exploded view of the dose counter shown in FIG. **23**;

FIG. **25** is an exploded view of parts of the inhaler of FIG. **21**; and

FIG. **26** is a view of a yoke of the inhaler of FIG. **21**.

DETAILED DESCRIPTION OF THE INVENTION

FIG. **1** shows a main body **10** of a manually operated metered dose inhaler **12** in accordance with an embodiment related to the present invention and having a mouthpiece cap **14** securable over a mouthpiece **16** of the main body.

The main body has a canister chamber **18** into which a canister **20** (FIG. **7**A) is slideable. The canister **20** has a generally cylindrical main side wall **24**, joined by a tapered section **26** to a head portion **28** having a substantially flat lower face **30** which has an outer annular drive surface **32** arranged to engage upon and drive an actuation pin **34** of a dose counter **36** as will be described. Extending centrally and axially from the lower face **30** is a valve stem **38** which is arranged to sealingly engage in a valve stem block **40** of the main body **10** of the inhaler **12**. The valve stem block **40** has a passageway **42** leading to a nozzle **44** for directing the contents of the canister **20**, namely active drug and propellant, towards an air outlet **46** of the inhaler main body **12**. It will be appreciated that due to gaps **48** between the canister **20** and an inner wall **50** of the main body **10** of the inhaler **12** an open top **52** of the main body **10** forms an air inlet into the inhaler **12** communicating via air passageway **54** with the air outlet **46**, such that canister contents exiting nozzle **44** mix with air being sucked by the user through the air passageway **54** in order to pass together through the air outlet and into the mouth of the user (not shown).

The dose counter **36** will now be described. The dose counter **36** includes an actuation pin **34** biased upwardly from underneath by a return spring **56** once installed in the main body **10**. As best shown in FIGS. **4**A, **6**H and **8**A, the pin **34** has side surfaces **58**, **60** arranged to slide between corresponding guide surfaces **62**, **64** located in a dose counter chamber **66** of the main body **10**, as well as an end stop surface **68** arranged to engage a corresponding end stop **70** formed in the dose counter chamber **66** to limit upward movement of the pin **34**. The pin **34** has a top part **72** which is circularly cylindrical and extends through an aperture **74** formed through a separator wall **76** which separates the canister chamber **18** from the dose counter chamber **66**. The top part **72** of the pin **34** has a flat top surface **78** which is arranged to engage the outer annular drive surface **32** of the canister **20**.

The actuation pin **34** is integrally formed with a drive or actuator pawl **80**. The actuator pawl **80** has a generally inverted U-shape configuration, having two mutually spaced and parallel arms **82**, **84** extending from a base portion of the actuation pin **34**, each holding at respective distal ends **88** thereof opposite ends of a pawl tooth member **90** which extends in a direction substantially perpendicular to the arms **82**, **84**, so as to provide what may be considered a "saddle" drive for pulling on each of the 11 drive teeth **92** of a ratchet wheel **94** of an incremental drive system **96** or ratchet mechanism **96** of the dose counter **36**. As shown for example in FIG. **10**B, the pawl tooth member **90** has a sharp lower

longitudinal side edge **98** arranged to engage the drive teeth **92**, the edge-to-surface contact provided by this engagement providing very accurate positioning of the actuator pawl **80** and resultant rotational positioning of the ratchet wheel **94**.

The dose counter **36** also has a chassis preassembly **100** which, as shown in FIGS. **4**A and **6**A, includes a chassis **102** having a first shaft **104** receiving the ratchet wheel **94** which is secured to a tape reel shaft **106**, and a second shaft (or split pin) **108** which is parallel to and spaced from the first shaft **104** and which slidably and rotationally receives a tape stock bobbin **110**.

As shown in FIG. **6**B, when the inhaler has not been used at all, the majority of a tape **112** is wound on the tape stock bobbin **110** and the tape **112** has a series of regularly spaced numbers **114** displayed therealong to indicate a number of remaining doses in the canister **20**. As the inhaler is repeatedly used, the ratchet wheel **94** is rotated by the actuator pawl **80** due to operation of the actuation pin **34** by the canister **20** and the tape **112** is incrementally and gradually wound on to the tape reel shaft **106** from the second shaft **108**. The tape **112** passes around a tape guide **116** of the chassis **102** enabling the numbers **114** to be displayed via a window **118** in a dose counter chamber cover **120** having a dose marker **132** formed or otherwise located thereon.

As shown in FIGS. **6**A and **6**D, the second shaft **108** is forked with two forks **124**, **126**. The forks **124**, **126** are biased away from one another. The forks have located thereon at diametrically opposed positions on the second shaft **108** friction or control elements **128**, **130**, one on each fork. Each control element extends longitudinally along its respective fork **124**, **126** and has a longitudinally extending friction surface **132**, **134** which extends substantially parallel to a longitudinal axis of the second shaft and is adapted to engage inside a substantially cylindrical bore **136** inside the tape stock bobbin **110**. This control arrangement provided between the bore **136** and the control elements **128**, **130** provides good rotational control for the tape stock bobbin **110** such that it does not unwind undesirably such as when the inhaler is dropped. The tape force required to unwind the tape stock bobbin **110** and overcome this friction force is approximately 0.1 N.

As can be seen in FIG. **6**D, as well as FIGS. **6**G and **10**A to **10**F, the chassis **102** is provided with an anti-back drive tooth **138** or count pawl **138** which is resiliently and substantially fixedly mounted thereto. As will be described below and as can be seen in FIGS. **10**A to **10**F, when the actuation pin **34** is depressed fully so as to fire the metered valve (not shown) inside the canister **20**, the actuator pawl **80** pulls down on one of the teeth **92** of the ratchet wheel **94** and rotates the wheel **94** anticlockwise as shown in FIG. **6**D so as to jump one tooth **92** past the count pawl **138**, thereby winding the tape **112** a distance incrementally relative to the dose marker **122** on the dose counter chamber **120** so as to indicate that one dose has been used.

With reference to FIG. **10**B, the teeth of the ratchet wheel **94** have tips **143** which are radiused with a 0.1 mm radius between the flat surfaces **140**, **142**. The ratchet wheel **94** has a central axis **145** which is 0.11 mm above datum plane **220** (FIG. **9**). A top/nose surface **147** of the anti-back drive tooth **138** is located 0.36 mm above the datum plane **220**. The distance vertically (i.e. transverse to datum plane **220**—FIG. **9**) between the top nose surface **147** of the anti-back drive tooth is 0.25 mm from the central axis **145** of the wheel **94**. Bump surface **144** has a lateral extent of 0.20 mm, with a vertical length of a flat **145'** thereof being 1 mm, the width of the bump surface being 1.22 mm (in the direction of the axis **145**), the top **149** of the bump surface **144** being 3.02 mm vertically below the axis **145**, and the flat **145'** being spaced a distance sideways (i.e. parallel to the datum plane **220**) 2.48 mm from the axis **145**. The top surface **78** of the pin **34** (FIG. **6**H) is 11.20 mm above the datum plane **220** (FIG. **9**) when the actuator pawl **80** and pin **34** are in the start configuration. The length of the valve stem **22** is 11.39 mm and the drive surface **32** of the canister **20** is 11.39 mm above the datum plane **220** when the canister is at rest waiting to be actuated, such that there is a clearance of 0.19 mm between the canister **20** and the pin **34** in this configuration.

FIGS. **10**A and **10**B show the actuator pawl **80** and ratchet wheel **94** and count pawl **138** in a start position in which the flat top **78** of the pin **34** has not yet been engaged by the outer annular drive surface **32** of the canister **20** or at least has not been pushed down during a canister depression.

In this "start" position, the count pawl **138** engages on a non-return back surface **140** of one of the teeth **92** of the ratchet wheel **94**. The lower side edge **98** of the actuator pawl is a distance "D" (FIG. **9**) 1.33 mm above datum plane **220** which passes through bottom surface or shoulder **41** of valve stem block **40**, the datum plane **220** being perpendicular to a main axis "X" of the main body **10** of the inhaler **12** which is coaxial with the centre of the valve stem block bore **43** and parallel to a direction of sliding of the canister **20** in the main body **10** of the inhaler **12** when the canister is fired.

As shown in FIG. **10**B, an advantageous feature of the construction is that the pawl tooth/actuator **90** acts as a supplementary anti-back drive member when the inhaler **12** is not being used for inhalation. In particular, if the inhaler **12** is accidentally dropped, resulting in a jolt to the dose counter **36** then, if the wheel **94** would try to rotate clockwise (backwards) as shown in FIG. **10**B, the back surface **140** of a tooth will engage and be blocked by the tooth member **90** of the pawl **80**. Therefore, even if the anti-back drive tooth **138** is temporarily bent or overcome by such a jolt, undesirable backwards rotation of the wheel **94** is prevented and, upon the next canister firing sequence, the pawl **90** will force the wheel **94** to catch up to its correct position so that the dose counter **36** continues to provide correct dosage indication.

FIG. **10**C shows a configuration in which the actuator pawl **80** has been depressed with the pin **34** by the canister **20** to a position in which the side edge **98** of the pawl tooth member **90** is just engaged with one of the teeth **92** and will therefore upon any further depression of the pin **34** begin to rotate the wheel **94**. This is referred to as a "Reset" position or configuration. In this configuration, the lower side edge **98** of the actuator **80** is 0.64 mm above the datum plane **220**.

FIG. **10**D shows a configuration in which the actuator pawl **80** has been moved to a position lower than that shown in FIG. **10**C and in which the metered dose valve (not shown) inside the canister has at this very position fired in order to eject active drug and propellant through the nozzle **44**. It will be noted that in this configuration the count pawl **138** is very slightly spaced from the back surface **140** of the same tooth **92** that it was engaging in the configuration of FIG. **10**D. The configuration shown in FIG. **10**D is known as a "Fire" configuration. In this configuration the lower side edge **98** of the actuator **80** is 0.47 min below the datum plane **220**.

FIG. **10**E shows a further step in the sequence, called a "Count" position in which the actuator pawl **80** has rotated the ratchet wheel **94** by the distance circumferentially angularly between two of the teeth **92**, such that the count pawl **138** has just finished riding along a forward surface **142** of one of the teeth **92** and has resiliently jumped over the tooth

into engagement with the back surface **140** of the next tooth. Accordingly, in this "Count" configuration, a sufficiently long stroke movement of the pin **34** has occurred that the tape **112** of the dose counter **36** will just have counted down one dose. In this configuration, the lower side edge **98** of the actuator is 0.95 mm below the datum plane **220**, Accordingly, in this position, the actuator **80** generally, including edge **98**, is 0.48 mm lower than in the fire configuration. It has been found that, although the count configuration happens further on than the fire configuration, counting is highly reliable, with less than 50 failed counts per million. This is at least partially due to momentum effects and to the canister releasing some back pressure on the user in some embodiments as its internal metering valve fires.

In the configuration of FIG. **10**F, the pawl **80** has been further depressed with the pin **34** by the canister **20** to a position in which it is just disengaging from one of the teeth **92** and the actuator pawl **80** is assisted in this disengagement by engagement of one of the arms **84** with a bump surface **144** on the chassis **102** (see FIG. **6**G) and it will be seen at this point of disengagement, which is called an "End" configuration, the count pawl **138** is positioned exactly halfway or substantially halfway between two of the drive teeth **92**. This advantageously means therefore that there is a minimum chance of any double counting or non-counting, which would be undesirable. In the end configuration, the side edge **98** of the actuator is 1.65 mm below the datum plane **220**. It will be appreciated that any further depression of the actuator pawl **80** and pin **34** past the "End" configuration shown in FIG. **10**F will have no effect on the position of the tape **112** displayed by the dose counter **36** since the actuator pawl **80** is disengaged from the ratchet wheel **94** when it is below the position shown in FIG. **10**F.

As shown in FIGS. **7**C and **7**D, the inner wall **50** of the main body **10** is provided with a two-step support rail **144** which extends longitudinally along inside the main body and is located directly adjacent the aperture **74**. As shown in FIG. **7**B a diametrically opposed two-step support rail **146** is also provided and this diametrically opposed in the sense that a vertical plane (not shown) can pass substantially directly through the first rail **144**, the aperture **74**, a central aperture **148** of the valve stem block **40** (in which canister stem **25** is located) and the second two-step support rail **146**. As shown in FIG. **7**A and schematically in FIG. **7**B, the rails **144**, **146** provide a maximum clearance between the canister **20** and the rails **144**, **146** in a radial direction of almost exactly 0.3 mm, about 0.25 to 0.35 mm being a typical range. This clearance in this plane means that the canister **20** can only rock backwards and forwards in this plane towards away from the actuation pin **34**. A relatively small distance and this therefore prevents the canister wobbling and changing the height of the actuation pin **34** *a* as to undesirably alter the accuracy of the dose counter **36**. This is therefore highly advantageous.

The inner wall **50** of the main body **10** is provided with two further two-step rails **150** as well as two pairs **152**, **154** of rails extending different constant radial amounts inwardly from the inner wall **50**, so as to generally achieve a maximum clearance of almost exactly 0.3 mm around the canister **20** for all of the rails PH, **146**, **150**, **152**, **154** spaced around the periphery of the inner wall **50**, in order to prevent undue rocking while still allowing canister motion freely inside the inhaler **12**. It will be clear from FIG. **7**C for example that the two-step rails have a first portion near an outlet end **156** of the canister chamber **18**, the first portion having a substantially constant radial or inwardly-extending width, a first step **160** leading to a second portion **162** of the rail, the second portion **102** having a lesser radial or inwardly extending extent than the first portion **156**, and finally a second step **164** at which the rail merges into the main inner wall **50** main surface.

A method of assembling the inhaler **12** will now be described.

With reference to FIG. **8**A, the main body **10** of the inhaler **12** is formed by two or more plastics mouldings which have been joined together to the configuration shown.

As shown in FIG. **8**B, the actuator pawl **80** and pin **34** are translated forward into position into a pin receiving area **166** in the dose counter chamber **66** and the pin **34** and actuator **80** may then be raised until the pin **34** emerges through the aperture **74**.

Next, the return spring **56** may be inserted below the pin **34** and a generally cylindrical annular lower end **168** of the spring **56** may be moved by a tweezer or tweezer-like assembly tool (not shown) into engagement with a shelf **170** of a spring retainer **172** in the dose counter chamber **66**. The spring retainer **172** is U-shaped and the shelf **170** is U-shaped and has a recess **174** formed below it. As shown in FIGS. **4**B, **4**C and **12** shelf **170** includes three chamfer surfaces **176**, **178**, **180** arranged to assist in moving the lower end of the spring **168** into position onto the shelf using the assembly tool (not shown). Once the lower end of the spring **168** is in place, the assembly tool (not shown) can easily be removed at least partly via the recess **174** below the lower end **168** of the spring **56**.

The tape **112** is attached at one end (not shown) to the tape stock bobbin **110** and is wound onto the bobbin by a motor **200** (FIG. **13**) having a hexagonal output shaft **202** which engages in a hexagonal socket **204** (FIG. **6**B) of the bobbin. During winding, the tape is monitored by a sensor **206**, which may be in the form of a camera or laser scanner, which feeds data to a computer controller **205** for the motor **200**. The controller **205** recognises three positioning markers **210** in the form of lines across the tape **112** and stops the motor **202** when the tape **112** is nearly fully wound onto the bobbin **110**, such that the distal end **212** of the tape **112** can be secured, e.g. by adhesive, to the tape reel shaft **106**. The controller **205** also recognises a pixelated tape size marker **214** observed by the sensor **206** and logs in a stocking system data store **217** details of the tape **112** such as the number of numbers **114** on the tape, such as one hundred and twenty or two hundred numbers **114**. Next, the tape reel shaft is wound until an appropriate position of the lines **210** at which a priming dot **216** will, once the bobbin **110** and reel shaft **106** are slid onto the second shaft **108** and second shaft **104**, be in a position to be located in the window **118** when the inhaler **12** is fully assembled. In the embodiments, the bobbin **110** and reel shaft **106** may be slid onto the shafts **108**, **104** before the tape **112** is secured to the reel shaft **106** and the reel shaft may then be wound to position the priming dot **216**.

Next, the assembled dose counter components of the chassis preassembly **100** shown in FIG. **6**B may as shown in FIG. **8**C be inserted into the dose counter chamber **66**, with pins **182**, **184**, **186** formed on the main body **10** in the dose counter chamber **66** passing through apertures or slots **188**, **190**, **192** formed on the chassis **102**, such that the pins **182**, **184**, **186** extend through (or at least into) the apertures or slots **188**, **190**, **192**. With the chassis **102** being relatively firmly pushed towards the main body **10**, the pins **182**, **184**, **186** are then heat staked and the chassis **102** is therefore after this held very firmly in position in the main body and is unable to move, thereby assisting in providing great accuracy for the dose counter **36**. Next, as shown in FIG. **8**D, the

dose counter chamber **120** may be fitted over the dose counter chamber **66** and may be secured in place such as by welding, with the priming dot **216** being displayed through the window.

The user can, when readying the inhaler **12** for first use, prime the inhaler by depressing the canister **20** three times which will bring the first number **114** on the tape into display through the window **118** in place of the priming dot **216**, the number **114** shown in FIG. **8**D being "200", thereby indicating that 200 doses are remaining to be dispensed from the canister **20** and inhaler **12**.

As shown in FIG. **8**D, and in FIG. **5**, an open drain hole **194** is provided at the bottom of the dose counter chamber **66** by a substantially semi-circular cut-out or recess formation **196** in a lower surface **198** of the main body **10** of the inhaler. Accordingly, if the user (not shown) should decide to wash the main body **10** of the inhaler, for example after encountering an unhygienic situation or simply as a matter of choice, the drain hole **194** allows initial draining of water from inside the dose counter chamber **66** and also thereafter evaporation of water or any aqueous matter in the dose counter chamber **66** so that the window **118** does not mist up undesirably.

FIG. **14** shows a computer system **230** for designing the dose counter **36** and in particular for calculating distributions representative of average positions and standard deviations in a production series of inhalers of the start, reset, fire, count and end positions of the actuator lower side edge **98** relative to the datum plane **220** (FIG. **9**) and therefore of the actuator pawl **80** generally relative to the ratchet wheel **94**, chassis **102** and, when the inhaler **12** is fully assembled, the main body **10** of the inhaler **12**. The computer system **230** includes a data store **232**, a CPU **234**, an input device **236** (such as a keyboard or communication port) and an output device **238** (such as a communications port, display screen and/or printer). A user may enter data via the input device **236** which may be used by the CPU **234** in a mathematical calculation to predict count failure rates when the various dose counters are to be built in a series with dose counter positions set with given averages and standard deviations and taking into account any momentum/inertia effects and metering valve user-back-pressure reduction effect which will occur upon canister firing of a given type of canister. The computer system **230** is thus mathematically used to design the distributions. For the inhaler **12** described herein with the dose counter **36** and canister **20**, the distributions are designed as shown in FIG. **11**. The x axis shows distance of the lower side surface **98** of the actuator **80** above the datum plane **220** and the y axis is representative of the distribution. Thus, curve **240** shows that the start configuration has an average 1.33 mm above the datum plane **200** (standard deviation is 0.1 mm), curve **242** shows that the reset configuration has an average of 0.64 mm above the datum plane **220** (standard deviation is 0.082 mm), curve **244** shows the fire configuration has an average 0.47 mm below the datum plane **220** (standard deviation is 0.141 mm), curve **246** shows the count configuration has an average 0.95 mm below the datum plane **220** (standard deviation is 0.080 mm), and curve **248** shows the end configuration has an average of 1.65 mm below the datum plane **220** (standard deviation is 0.144 mm).

FIGS. **15** to **20** show a version of the inhaler modified in accordance with the present invention. In these drawings, the same reference numerals have been used to those in the earlier drawings to denote the equivalent components. The inhaler **12** is the same as that in FIGS. **1** to **14** apart from the following modifications.

First, it can be seen that there is a modification in that the drive teeth **92** of the ratchet wheel **94** have a different profile to that in FIGS. **1** to **14**. There are also only nine ratchet teeth **94** in this embodiment instead of eleven.

Additionally, as shown in FIGS. **18**C and **19**C, the control elements **128**, **130** on the forks **124**, **126** of the second shaft **108** have a tapered profile which is different to the profile of the control elements **128**, **130** shown in FIG. **6**F. Either profile can be used in the embodiment of FIGS. **15** to **20** however.

Furthermore, as shown in FIG. **15**, the tape stock bobbin **110** has an inwardly facing generally cylindrical engagement surface **300** with a wavelike form extending partially therealong. The engagement surface **300** has a cross-section **301** perpendicular to the longitudinal length of the stock bobbin **110** which is constant therealong. This cross-section **301** can be seen in FIG. **16** and consists of a series of ten regularly spaced concavities **302** and ten convex wall portions **304**. The convex wall portions **304** are equi-spaced between the concavities **302**. Each concavity **302** has a radius of 0.2 mm. Each convex wall portion **304** also has a radius of 0.2 mm. Finally, the cross section **301** also includes flat wall portions **306** between all of the radiused wall portions of the concavities **302** and convex wall portions **304**. The geometry of the cross-section **301** is therefore defined by the radii of the concavities **302** and convex wall portions **304**, the flat wall portions **306** and the fact that there are ten concavities **302** and convex wall portions **304**.

The minor diameter of the engagement surface **300**, i.e. between the tips of opposite convex wall portions **304**, is 2.46 mm. The major diameter of the engagement surface **300**, i.e. between the outermost portions of the concavities **302**, is 2.70 mm. The undeformed tip to tip maximum diameter of the forks **124**, **126** of the split pin (the second shaft) **108**, i.e. in the region of the maximum radio extent of the control elements **128**, **130**, is 3.1 millimetres and it will therefore be appreciated that the forks **124**, **126** are resiliently compressed once the stock bobbin **110** has been assembled onto the split pin **108** in all rotational configurations of the stock bobbin **110** relative to the split pin **108**. The minimum gap between the forks **124**, **126** in the plane of the cross sections of FIGS. **18**C and **19**C is 1 mm when the split pin **108** is in the undeformed, pre-inserted state. When the split pin **108** is at maximum compression, as shown in FIGS. **18**A to **18**C when the control elements **128**, **130** are shown to be engaged on top of the convex wall portions **304**, the gap **308** between the tips **310**, **312** of the forks **124**, **126** is 0.36 mm. On the other hand, when the split pin **108** is at minimum compression (once inserted into the stock bobbin) as shown in FIGS. **19**A to **19**C, when the control elements **128**, **130** rest in the concavities **302**, the gap between the tips **310**, **312** of the forks **124**, **126** is 0.6 mm. The control elements **128**, **130** are outwardly radiused with a radius also of 0.2 mm such that they can just rest on the concavities **302** with full surface contact (at least at an axial location on the split pin where the tapered control elements are at their maximum radial extent), without rattling in, locking onto or failing to fit in the concavities **302**. The radii of the control elements **128**, **130** is therefore preferably substantially the same as the radii of the concavities **302**

It will be appreciated that whereas FIGS. **18**B and **19**B are end views along the coaxial axis of the stock bobbin **110** and split pin **108**, FIGS. **18**A and **19**A are cross-sections. FIG. **19**A is a section on the plane A-A' in FIG. **19**C and FIG. **18**A is a section at the same plane, but of course with the stock bobbin **110** rotated relative to the split pin **108**.

As the inhaler **12** is used and the ratchet wheel **94** rotates in order to count used doses, the stock bobbin rotates incrementally through rotational positions in which rotation is resisted, i.e. due to increasing compression of the split pin **108** at such rotational positions, and rotational positions in which rotation is promoted, i.e. due to decreasing compression of the split pin **108** at such rotational positions and this may involve a click forward of the stock bobbin **110** to the next position equivalent to that in FIGS. **19**A to **19**C in which the control elements **128**, **130** of the split pin art located in the concavities **302**. This functionality firstly allows the stock bobbin to unwind during use as required, but also prevents the tape **112** from loosening during transit if the inhaler **12** is dropped, such as onto a hard surface. This is highly advantageous, since the tape **11** is prevented from moving to a position in which it will give an incorrect reading regarding the number of doses in the canister.

During compression and expansion of the forks in the radial direction between the two configurations shown in FIGS. **18**C and **19**C, the forks **124**, **126** rotate about a point **316** on the split pin where the forks **124**, **126** come together. This rotational action means that there is a camming action between the forks **124**, **126** and the engagement surface **300** without significant friction but, nevertheless, the resilient forces provided by the regulator formed by the engagement surface **300** and forks **124**, **126** are able to regulate unwinding of the tape such that it does not easily occur during transit or if the inhaler **12** is dropped. It has been found during testing that a force of 0.3 to 0.4 N needs to be applied to the tape **112** to overcome the regulator at the stock bobbin **110**. 0.32 N is achieved with the control elements **128** having the profile shown in FIG. **19**C and 0.38 N is achieved with the profile of the control elements **128** altered to be as shown as described with reference to FIG. **6**F. These forces are substantially higher than the 0.1 N force mentioned above and undesirable movement of the tape is substantially avoided even if the inhaler is dropped onto a hard surface. The modified arrangement of FIGS. **15** to **20** does not provide this force "constantly" such that there is overall not an undesirably high friction of the tape **112** as it passes over the other components of the dose counter because, due to the incremental nature of the resilient forces at the regulator, the tape **112** can incrementally relax as it slides over the stationary chassis components.

Instead of having ten concavities **302** and convex wall portions **304**, other numbers may be used, such as 8 or 12. However, it is preferred to have an even number, especially since two control elements **128**, **130** are provided, so that all of the control elements **128**, **130** will expand and contract simultaneously. However, other arrangements are envisaged with 3 or more forks and the number of concavities/convex wall portions may be maintained as an integer divisible by the number of forks to maintain a system with simultaneous expansion/contraction. For example, the use of 9, 12 or 15 concavities/convex wall portions with 3 forks is envisaged.

Instead of having the engagement surface **300** on the inside of the stock bobbin **110**, it could be placed on the outside of the stock bobbin **110** so as to be engaged by flexible external legs/pawls or similar.

It will be noted that the regulator provided by the engagement surface **300** and forks **124**, **126** does not only allow rotation of the stock bobbin in one direction as is the case with the ratchet wheel **94**. Rotation in both directions is possible, i.e. forwards and backwards. This means that during assembly, the stock bobbin **110** can be wound backwards during or after fitting the bobbin **100**, shaft **106** and tape **112** onto the carriage **102**, if desired.

The stock bobbin **110** and the carriage **102** including the split pin **108** are both moulded of polypropylene material.

It will be seen from FIG. **16** that the cross-sectional shape **301** is not symmetrical within the hexagonal socket **204**. This has enabled the hexagonal socket **204** to be maintained at a useful size while still allowing the desired size and geometry of the cross section **301** to fit without interfering with the hexagonal shape of the hexagonal socket **204** and also permits moulding to work during manufacture.

As shown in FIG. **17**, the stock bobbin **110** has a series of four circumferential ribs **330** inside it and a spaced thereabout. These hold the stock bobbin **110** on the correct side of the mould tool during moulding.

FIGS. **21** and **22** show a preferred embodiment in accordance with the invention of an inhaler **510** for dispensing a dry-powdered medicament in metered doses for patient inhalation. The inhaler **510** is as disclosed in FIGS. **1** to **16** or EP-A-1330280, the contents of which are hereby fully incorporated herein by reference, but with the stock bobbin **110** and second shaft **108** of the dose counter **516** modified so as to be as in FIGS. **15** to **20** hereof. Thus, the dry powder inhaler **510** generally includes a housing **518**, and an assembly **512** received in the housing (see FIG. **21**). The housing **518** includes a case **520** having an open end **522** and a mouthpiece **524** (FIG. **25**) for patient inhalation, a cap **526** secured to and closing the open end **522** of the case **520**, and a cover **528** pivotally mounted to the case **520** for covering the mouthpiece **524**. As shown in FIG. **22**, the inhaler **510** also includes an actuation spring **569**, first yoke **566** with opening **572**, bellows **540** with crown **574**, a reservoir **514**, second yoke **568** with hopper **542** and dose counter **516** mounted thereto, and case **520** has transparent window **5130** thereon for viewing dose counter tape indicia **5128**. The dose metering system also includes two cams **570** mounted on the mouthpiece cover **528** and movable with the cover **528** between open and closed positions. The cams **570** each include an opening **580** for allowing outwardly extending hinges **582** of the case **520** to pass therethrough and be received in first recesses **584** of the cover **528**. The cams **570** also include bosses **586** extending outwardly and received in second recesses **588** of the cover **528**, such that the cover **528** pivots about the hinges **582** and the cams **570** move with the cover **528** about the hinges **582**. As described in EP-A-1330280, cams **570** act upon cam followers **578** to move second yoke **568** up and down and thereby operate dose counter by engagement of pawl **5138** on the second yoke **568** with teeth **5136**. Remaining components of the inhaler are provided as, and operate as described, in EP-A-1330280.

The dose counting system **516** therefore includes a ribbon or tape **5128** (FIGS. **23** & **24**), having successive numbers or other suitable indicia printed thereon, in alignment with a transparent window **5130** provided in the housing **18** (see FIG. **22**). The dose counting system **516** includes the rotatable stock bobbin **110** (as described above), an indexing spool **5134** rotatable in a single direction, and the ribbon **5128** rolled and received on the bobbin **110** and having a first end **5127** secured to the spool **5134**, wherein the ribbon **5128** unrolls from the bobbin **110** so that the indicia are successively displayed as the spool **5134** is rotated or advanced. In FIGS. **23** and **24** the wavelike engagement surface **300** of the bobbin **110** is not shown for the purposes of clarity.

The spool **134** is arranged to rotate upon movement of the yokes **566**, **568** to effect delivery of a dose of medicament from reservoir **514**, such that the number on the ribbon **5128** is advanced to indicate that another dose has been dispensed by the inhaler **510**. The ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase or

decrease upon rotation of the spool **5134**. For example, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, decrease upon rotation of the spool **5134** to indicate the number of doses remaining in the inhaler **510**. Alternatively, the ribbon **5128** can be arranged such that the numbers, or other suitable indicia, increase upon rotation of the spool **5134** to indicate the number of doses dispensed by the inhaler **10**.

The indexing spool **5134** includes radially extending teeth **5136**, which are engaged by pawl **5138** extending from a cam follower **578** of the second yoke **568** upon movement of the yoke to rotate, or advance, the indexing spool **5134**. More particularly, the pawl **5138** is shaped and arranged such that it engages the teeth **5136** and advances the indexing spool **5134** only upon the mouthpiece cover **528** being closed and the yokes **566**, **568** moved back towards the cap **526** of the housing **518**.

The dose counting system **516** also includes a chassis **5140** that secures the dose counting system to the hopper **542** and includes shafts **108**, **5144** for receiving the bobbin **110** and the indexing spool **5134**. As described above with reference to FIGS. **1** to **20**, the bobbin shaft **108** is forked and includes radially nubs **5146** for creating a resilient resistance to rotation of the bobbin **110** on the shaft **108** by engaging with the wavelike engagement surface **300** inside the bobbin **110**. A clutch spring **5148** is received on the end of the indexing spool **5134** and locked to the chassis **5140** to allow rotation of the spool **5134** in only a single direction.

Various modifications may be made to the embodiment shown without departing from the scope of the invention as defined by the accompanying claims as interpreted under patent law.

What is claimed is:

1. An incremental dose counter for a metered dose inhaler having a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body, an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction, such that the actuator acts as an anti-back drive member when the actuator is in a non-depressed position, and wherein the incremental dose counter further comprises a second anti-back member configured to restrict motion of the output member in a direction opposite to the count direction when the actuator is disengaged from the output member by a bump surface.

2. The incremental dose counter as claimed in claim **1** in which the output member comprises a ratchet wheel.

3. The incremental dose counter as claimed in claim **2** in which the actuator comprises a pawl and in which the ratchet wheel and pawl are arranged to permit only one way ratcheting motion of the ratchet wheel relative to the pawl.

4. The incremental dose counter as claimed in claim **3** wherein the second anti-back member is fixed to the main body.

5. The incremental dose counter as claimed in claim **4** in which, when in a rest position of the dose counter, the ratchet wheel is capable of adopting a configuration in which a back surface of one tooth thereof engages the second anti-back member and the pawl is spaced from an adjacent back surface of another tooth of the ratchet wheel without positive drive/blocking engagement between the pawl and ratchet wheel.

6. A dose counter as claimed in claim **1** wherein an incremental counting system is arranged to move a counter display incrementally in a first direction from a first station to a second station in response to actuation input, wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

* * * * *

Rebekah Conroy
STONE CONROY LLC
25 A Hanover Road, Suite 301
Florham Park, NJ 07932
Tel: (973) 400-4181
Fax: (973) 498-0070
rconroy@stoneconroy.com

Of counsel (Pro Hac vice Forthcoming)
Steven Maddox
Jeremy J. Edwards
PROCOPIO
1050 Connecticut Ave, NW
Suite 500
Washington, DC 20036
steven.maddox@procopio.com
jeremy.edwards@procopio.com

Attorneys for Defendants

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., and TEVA PHARMACEUTICALS USA, INC. Plaintiffs, v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS LLC, and AMNEAL PHARMACEUTICALS INC. Defendants.	Civil Action No. 23-cv-20964-JXN-MAH **JURY TRIAL DEMANDED**

AMNEAL PHARMACEUTICALS OF NEW YORK, LLC; AMNEAL IRELAND LIMITED; AMNEAL PHARMACEUTICALS LLC; and AMNEAL PHARMACEUTICALS INC.'S ANSWER, AFFIRMATIVE DEFENSES, AND COUNTERCLAIMS TO PLAINTIFFS' FIRST AMENDED COMPLAINT

Defendants Amneal Pharmaceuticals of New York, LLC; Amneal Ireland Limited; Amneal Pharmaceuticals LLC; and Amneal Pharmaceuticals Inc. (collectively, "Defendants"), by and through their undersigned counsel, for their Answer to the First Amended Complaint filed by Plaintiffs Teva Branded Pharmaceutical Products R&D, Inc. ("Teva Branded"), Norton (Waterford) Ltd. ("Norton"), and Teva Pharmaceuticals USA, Inc. ("Teva USA") (collectively, "Plaintiffs"), and their Counterclaims against Plaintiffs, hereby state as follows:

GENERAL DENIAL

Pursuant to Federal Rule of Civil Procedure 8(b)(3), Defendants deny all allegations in Plaintiffs' First Amended Complaint except those specifically admitted below.

NATURE OF THE ACTION

1. This is an action for patent infringement under the patent laws of the United States, 35 U.S.C. § 100 *et seq.*, including 35 U.S.C. § 271, the Drug Price Competition and Patent Term Restoration Act of 1984, 21 U.S.C. § 355(j) ("Hatch-Waxman Act"), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, that arises out of Amneal's submission of Abbreviated New Drug Application ("ANDA") No. 211600 to the U.S. Food and Drug Administration ("FDA") seeking approval to commercially manufacture, use, offer for sale, sell, and/or import a generic version of ProAir® HFA (albuterol sulfate) Inhalation Aerosol prior to the expiration of U.S. Patent Nos. 8,132,712 ("the '712 patent"), 9,463,289 ("the '289 patent"), 9,808,587 ("the '587 patent"), 10,561,808 ("the '808 patent"), and 11,395,889 ("the '889 patent"). Collectively, the '712 patent, the '289 patent, the '587 patent, the '808 patent, and the '889 patent are referred to herein as the "Patents-in-Suit."

ANSWER: Amneal admits that Counts I, III, V, VII, and IX of the First Amended Complaint purport to state causes of action for patent infringement under 35 U.S.C. § 271(e).

Amneal admits that Counts II, IV, VI, VIII, and X of the First Amended Complaint purport to state causes of action under the Declaratory Judgment Act for alleged potential patent infringement under 35 U.S.C. § 271(a). Amneal admits that this action arises out of one or more of the Plaintiffs having improperly caused the "Patents-in-Suit" to become listed for ProAir® HFA (albuterol sulfate) Inhalation Aerosol in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"), Amneal's subsequent submission of ANDA No. 211600 ("Amneal's ANDA") seeking FDA approval to market Amneal's generic version of ProAir® HFA prior to expiration of the Patents-in-Suit, and Plaintiffs' decision to sue Defendants within 45 days after receiving notice of Amneal's Paragraph IV filing, triggering a 30-month stay of final FDA approval of Amneal's ANDA pursuant to 21 U.S.C. § 355(j)(5)(B)(iii). Amneal denies the remaining allegations in paragraph 1.

THE PARTIES

Plaintiffs

2. Plaintiff Teva Branded is a company organized under the laws of the State of Delaware with its principal place of business at 145 Brandywine Parkway, West Chester, Pennsylvania 19380. In addition, Teva Branded has a place of business at 400 Interpace Parkway #3, Parsippany, New Jersey 07054.

ANSWER: On information and belief, admitted.

3. Plaintiff Norton is a private limited company organized under the laws of the Republic of Ireland and having its registered office at Unit 301, IDA Industrial Park, Waterford X91 WK68, Republic of Ireland. Norton trades, *i.e.*, does business, as Ivax Pharmaceuticals Ireland and as Teva Pharmaceuticals Ireland.

ANSWER: On information and belief, admitted.

4. Plaintiff Teva USA is a company organized and existing under the laws of the State of Delaware, with a principal place of business at 400 Interpace Parkway, Parsippany, New Jersey 07054.

ANSWER: On information and belief, admitted.

Defendants

5. On information and belief, Defendant Amneal NY is a limited liability company organized and existing under the laws of the State of Delaware, having a principal place of business at 400 Crossing Boulevard, 3rd Floor, Bridgewater, New Jersey 08807. On information and belief, Amneal NY is a wholly-owned subsidiary of Amneal Pharma. On further information and belief, Amneal NY is the U.S. agent for Amneal Ireland.

ANSWER: Admitted.

6. On information and belief, Defendant Amneal Ireland is a company organized and existing under the laws of Ireland, having a place of business at Cahir Road, Cashel, Co. Tipperary, Ireland E25 XD5l.

ANSWER: Admitted.

7. On information and belief, Defendant Amneal Pharma is a limited liability company organized and existing under the laws of Delaware, having a principal place of business at 400 Crossing Boulevard, 3rd Floor, Bridgewater, New Jersey 08807. On information and belief, Amneal Pharma is a wholly-owned subsidiary of Amneal Inc.

ANSWER: Admitted.

8. On information and belief, Defendant Amneal Inc. is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 400

Crossing Boulevard, 3rd Floor, Bridgewater, New Jersey 08807.

ANSWER: Admitted.

9. On information and belief, Defendants operate as a single vertically-integrated business with respect to the regulatory approval, manufacturing, marketing, sale and distribution of pharmaceutical products throughout the United States, including in this District. *See* Amneal Pharmaceuticals, Inc., Form 10-K for 2022 Fiscal Year, at 6-8 https://s22.q4cdn.com/186279204/files/doc_financials/2023/07/Amneal-2022-Form-10-K-asfiled.pdf (last visited October 6, 2023).

ANSWER: Admitted.

10. By a letter dated August 24, 2023 ("Amneal Notice Letter"), Defendant Amneal NY notified Plaintiffs that Amneal NY and Amneal Ireland had submitted to FDA Amneal's ANDA for a purported generic version of ProAir® HFA (albuterol sulfate) Inhalation Aerosol, 90 mcg per actuation ("Amneal ANDA Products"), seeking FDA approval to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of the Amneal ANDA Products in and/or into the United States, including New Jersey, prior to the expiration of the Patents-in-Suit.

ANSWER: Admitted.

11. On information and belief, Defendants acted in concert to prepare and submit Amneal's ANDA and the Amneal Notice Letter.

ANSWER: Denied.

JURISDICTION AND VENUE

Subject Matter Jurisdiction

12. Plaintiffs incorporate each of the preceding paragraphs 1–11 as if fully set forth herein.

ANSWER: Defendants incorporate each of its answers to preceding paragraphs 1–11 as if fully set forth herein.

13. This is a civil action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 100 *et seq.*, including 35 U.S.C. § 271.

ANSWER: Defendants incorporate their answer to paragraph 1 as if set forth herein.

14. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

ANSWER: Denied.

Personal Jurisdiction

15. Plaintiffs incorporate each of the preceding paragraphs 1–14 as if fully set forth herein.

ANSWER: Defendants incorporate each of its answers to preceding paragraphs 1–14 as if fully set forth herein.

16. Based on the facts and causes alleged herein, and for additional reasons to be further developed through discovery if necessary, this Court has personal jurisdiction over Defendants.

ANSWER: Paragraph 16 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 16 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court. Otherwise denied.

17. This Court has personal jurisdiction over Defendants because, among other things, Defendants have purposefully availed themselves of the benefits and protections of New Jersey's laws such that they should reasonably anticipate being haled into court here. On information and belief, Defendants develop, manufacture, import, market, offer to sell, sell, and/or import generic drugs throughout the United States, including in New Jersey, and therefore transact business within New Jersey, and/or have engaged in systematic and continuous business contacts within New Jersey.

ANSWER: Paragraph 17 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 17 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court. Otherwise denied.

18. In addition, this Court has personal jurisdiction over Defendants because, among other things, on information and belief: (1) Defendants filed Amneal's ANDA for the purpose of seeking approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products in the United States, including in New Jersey; and (2) upon approval of Amneal's ANDA, Defendants, individually and/or in concert, will market, distribute, offer for sale, sell, and/or import the Amneal ANDA Products in the United States, including in New Jersey, and will derive substantial revenue from the use or consumption of the Amneal ANDA Products in New Jersey. *See Acorda Therapeutics Inc. v. Mylan Pharm. Inc.*, 817 F.3d 755, 763 (Fed. Cir. 2016). On information and belief, upon approval of Amneal's ANDA, the Amneal ANDA Products will, among other things, be marketed, distributed, offered for sale, sold, and/or imported in New Jersey; prescribed by physicians practicing in New Jersey; dispensed by pharmacies located within New Jersey; and/or used by patients in New Jersey, all of which would have a substantial effect on New Jersey.

ANSWER: Paragraph 18 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 18 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court. Otherwise denied.

19. On information and belief, this Court also has personal jurisdiction over Defendant Amneal Inc. because it has its principal place of business in New Jersey.

ANSWER: Paragraph 19 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 19 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court, and Defendants admit that Amneal, Inc. has a principal place of business in New Jersey. Otherwise denied.

20. On information and belief, this Court also has personal jurisdiction over Defendant Amneal Pharma because it has its principal place of business in New Jersey.

ANSWER: Paragraph 20 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 20 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court, and Defendants admit that Amneal Pharma has a principal place of business in New Jersey. Otherwise denied.

21. On information and belief, this Court also has personal jurisdiction over Defendant Amneal NY because it has its principal place of business in New Jersey.

ANSWER: Paragraph 21 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 21 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court, and Defendants admit that Amneal NY has a principal place of business in New Jersey. Otherwise denied.

22. On information and belief, this Court also has personal jurisdiction over Defendant

Amneal Ireland because its U.S. agent, Amneal NY, has its principal place of business in New Jersey. On information and belief, Amneal Ireland acts through its U.S. agent Amneal NY.

ANSWER: Paragraph 22 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 22 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court, and Defendants admit that Amneal NY has a principal place of business in New Jersey. Otherwise denied.

23. The Amneal Notice Letter was sent by Bryan Sommese, Esq., Senior Patent Litigation Counsel – IP, for Amneal Pharma in Bridgewater, New Jersey, on behalf of Amneal NY and Amneal Ireland.

ANSWER: Defendants admit that the Amneal Notice Letter was signed by Bryan Sommese, Esq., Senior Patent Litigation Counsel – IP, for Amneal Pharmaceuticals of New York. Otherwise denied.

24. On information and belief, one or more acts related to Amneal's preparation of Amneal's ANDA were conducted in this District and/or will be conducted in the District.

ANSWER: Admitted.

25. On information and belief, Defendant Amneal Inc.'s corporate headquarters is located in Bridgewater, New Jersey.

ANSWER: Admitted.

26. On information and belief, Defendant Amneal NY is registered as "Manufacturer and Wholesale" with the State of New Jersey's Department of Health under Registration No. 5003663, originally issued on October 7, 2008.

ANSWER: Admitted.

27. On information and belief, Defendant Amneal Pharma is registered as "Manufacturer and Wholesale" with the State of New Jersey's Department of Health under Registration No. 5002991, originally issued on April 3, 2003. The Registered Addresses include 131 Chambers Brook Rd., Branchburg, NJ 08876; 1 New England Ave, Piscataway, NJ 08854; 1 Murray Rd, East Hanover, NJ 07936; 19 Readington Rd., Branchburg, NJ 08876; 47 Colonial Dr., Piscataway, NJ 08854; 21 Colonial Dr., Piscataway, NJ 08854; 400 Crossing Blvd., 3rd Fl., Bridgewater, NJ 08807; and 65 Readington Rd., Branchburg, NJ 08876.

ANSWER: Admitted as to Amneal Pharmaceuticals LLC. Otherwise denied.

28. On information and belief, Defendant Amneal Pharma is registered with the State of New Jersey's Department of the Treasury, Division of Revenue and Enterprise Services as a business operating in New Jersey under Business ID No. 0600211542.

ANSWER: Admitted as to Amneal Pharmaceuticals LLC. Otherwise denied.

29. On information and belief, Defendant Amneal Pharma leases at least ten (10) significant properties in New Jersey for the purposes of its executive offices, R&D, manufacturing, packaging, and warehousing, including in Bridgewater, Piscataway, Branchburg, and East Hanover. *See* Amneal Pharmaceuticals, Inc., Form 10-K for 2022 Fiscal Year, at 46 https://s22.q4cdn.com/186279204/files/doc_financials/2023/07/Amneal-2022-Form-10-K-as-filed.pdf (last visited October 6, 2023).

ANSWER: Admitted that Amneal Pharmaceutical, Inc. leases ten properties in New Jersey that are identified on the cited page of the cited Form 10-K as "significant properties," and that the "Purpose" listed on the cited page of the cited Form 10-K for at least one of those properties is "Executive Office," "Warehouse," "Manufacturing," "Packaging," and "R&D." Admitted that as of the time of the preparation of this answer, the cited Form 10-K was available at the cited web

address. Defendants lack information sufficient to form a belief as to when Plaintiffs "last visited" that web address, and on that basis deny such allegation. Otherwise denied.

30. In addition, this Court has personal jurisdiction over Defendants Amneal Ireland and Amneal NY because, on information and belief, Amneal NY, the U.S. agent of Amneal Ireland, regularly (1) engages in patent litigation concerning its ANDA Products in this District; (2) does not contest personal jurisdiction in this District; and (3) purposefully avails itself of the rights and benefits of this Court by asserting claims and/or counterclaims in this District. *See*, *e.g.*, Answer (Dkt. 11) ¶¶ 23-39, Counterclaims, *Therapeutics MD, Inc. v. Amneal Pharms., Inc. et al.*, Civil Action No. 3:20-cv-05256-FLW-TJB (D.N.J. filed July 7, 2020) (not contesting personal jurisdiction in this District and asserting counterclaims); Answer (Dkt. 14) ¶¶ 20, 26, *Janssen Products, LP et al. v. Amneal Pharmaceuticals LLC et al.*, No. 2:18-cv-17585-WHW- CLW (D.N.J. filed March 4, 2019) ("Amneal admits that Amneal NY has not contested personal jurisdiction in this District in several previous matters, solely for the purposes of those prior litigations and their specific subject matter."); Answer (Dkt. 87) ¶ 164, *BTG international Limited et al. v. Actavis Laboratories FL, Inc. et al.*, Case No. 2:15-cv-05909-KM-JBC (D.N.J. filed Oct. 15, 2015) ("Amneal does not object to this Court's personal jurisdiction over Amneal Pharmaceuticals and Amneal New York for the purposes of this action only.").

ANSWER: Paragraph 30 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 30 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court. Otherwise denied.

31. In addition, this Court has personal jurisdiction over Defendant Amneal Pharma because, on information and belief, Amneal Pharma regularly (1) engages in patent litigation concerning its ANDA Products in this District; (2) does not contest personal jurisdiction in this

District; and (3) purposefully avails itself of the rights and benefits of this Court by asserting claims and/or counterclaims in this District. *See, e.g.*, Answer (Dkt. 11) ¶¶ 23-39, Counterclaims, *Therapeutics MD, Inc. v. Amneal Pharms., Inc. et al.*, No. 3:20-cv-05256-FLW- TJB (D.N.J. filed July 7, 2020) (not contesting personal jurisdiction in this District and asserting counterclaims); Answer (Dkt. 14) ¶ 16, *Janssen Products, LP et al. v. Amneal Pharmaceuticals LLC et al.*, No. 2:18-cv-17585-WHW-CLW (D.N.J. filed March 4, 2019) ("Amneal LLC admits that it has not contested personal jurisdiction in this District in several previous matters solely for the purposes of those prior litigations and their specific subject matter."); Answer (Dkt. 87) ¶ 164, *BTG international Limited et al. v. Actavis Laboratories FL, Inc. et al.*, Case No. 2:15-cv- 05909-KM-JBC (D.N.J. filed Oct. 15, 2015) ("Amneal does not object to this Court's personal jurisdiction over Amneal Pharmaceuticals and Amneal New York for the purposes of this action only.").

ANSWER: Paragraph 31 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 31 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court. Otherwise denied.

32. In addition, this Court has personal jurisdiction over Defendant Amneal Inc. because, on information and belief, Amneal Inc., directly or indirectly through its subsidiaries including Amneal Pharma and Amneal NY, regularly (1) engages in patent litigation concerning its ANDA Products in this District; (2) does not contest personal jurisdiction in this District; and (3) purposefully avails itself of the rights and benefits of this Court by asserting claims and/or counterclaims in this District. *See* Answer (Dkt. 11) ¶¶ 23-39, Counterclaims, *Therapeutics MD, Inc. v. Amneal Pharms., Inc. et al.*, No. 3:20-cv-05256-FLW-TJB (D.N.J. filed July 7, 2020) (Amneal Inc. not contesting personal jurisdiction in this District and asserting counterclaims); *see also, e.g.*, Answer (Dkt. 14) ¶ 16, *Janssen Products, LP et al. v. Amneal Pharmaceuticals LLC et*

al., No. 2:18-cv-17585-WHW-CLW (D.N.J. filed March 4, 2019) ("Amneal LLC admits that it has not contested personal jurisdiction in this District in several previous matters solely for the purposes of those prior litigations and their specific subject matter."); Answer (Dkt. 87) ¶ 164, *BTG international Limited et al. v. Actavis Laboratories FL, Inc. et al.*, Case No. 2:15-cv- 05909-KM-JBC (D.N.J. filed Oct. 15, 2015) ("Amneal does not object to this Court's personal jurisdiction over Amneal Pharmaceuticals and Amneal New York for the purposes of this action only.").

ANSWER: Paragraph 32 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 32 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court. Otherwise denied.

33. For the above reasons, it would not be unfair or unreasonable for Defendants to litigate this action in this District, and the Court has personal jurisdiction over Defendants here.

ANSWER: Paragraph 33 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 33 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court. Defendants deny the allegation that it would not be unfair or unreasonable for Defendants to litigate this action. Otherwise denied.

34. In the alternative, Defendant Amneal Ireland is subject to personal jurisdiction in this forum because the requirements of Federal Rule of Civil Procedure 4(k)(2) are met as (a) Plaintiffs' claims arise under federal law; (b) Amneal Ireland is a foreign defendant not subject to general personal jurisdiction in the courts of any state; and (c) Amneal Ireland has sufficient contacts in the United States as a whole, including, but not limited to, by participating in the preparation and submission of Amneal's ANDA, and/or manufacturing, importing, offering to sell, or selling pharmaceutical products that are distributed throughout the United States, including in this District, such that this Court's exercise of jurisdiction over Amneal Ireland satisfies due

process.

ANSWER: Paragraph 34 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 34 is required, for purposes of this action only, Defendants do not contest personal jurisdiction in this Court. Otherwise denied.

Venue

35. Plaintiffs incorporate each of the preceding paragraphs 1–34 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–34 as if fully set forth herein.

36. Venue is proper in this Judicial District under 28 U.S.C. §§ 1391 and 1400(b).

ANSWER: Paragraph 36 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 36 is required, for purposes of this action only, Defendants do not contest venue in this Judicial District. Otherwise denied.

37. On information and belief, Defendants have a regular and established place of business in this District and have committed and/or will commit acts of infringement in this District. *See* 28 U.S.C. § 1400(b).

ANSWER: Denied.

38. On information and belief, Defendants have committed or aided, abetted, contributed to, and/or participated in the commission of, acts of infringement of the Patents-in-Suit by, among other things, preparing or assisting in preparing Amneal's ANDA in New Jersey and/or seeking to market the Amneal ANDA Products throughout the United States, including within New Jersey.

ANSWER: Denied.

39. On information and belief, Defendants (1) engage in patent litigation concerning their ANDA Products in this District, and (2) do not contest venue in this District. *See, e.g.*, Answer (Dkt. 11) ¶ 39, *Therapeutics MD, Inc. v. Amneal Pharms., Inc. et al.*, No. 3:20-cv- 05256-FLW-TJB (D.N.J. filed July 7, 2020) (Amneal Inc., Amneal Pharma, and Amneal NY, the U.S. agent of Amneal Ireland, not contesting that venue is proper in this District); Answer (Dkt. 14) ¶¶ 59, 60, *Janssen Products, LP et al. v. Amneal Pharmaceuticals LLC et al.*, No. 2:18-cv- 17585-WHW-CLW (D.N.J. filed March 4, 2019) (Amneal Pharma and Amneal NY, the U.S. agent of Amneal Ireland, not contesting venue in this District); Answer (Dkt. 87) ¶ 143, *BTG international Limited et al. v. Actavis Laboratories FL, Inc. et al.*, Case No. 2:15-cv-05909-KM-JBC (D.N.J. filed Oct. 15, 2015) (same).

ANSWER: Paragraph 39 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 39 is required, for purposes of this action only, Defendants do not contest venue in this District. Defendants admit that at least some of the Defendants have engaged in patent litigation in this District without contesting venue. Otherwise denied.

40. On information and belief, Defendant Amneal Inc. has a regular and established place of business in this District at least because it: (1) has a principal place of business in the State of New Jersey; (2) has acted in concert with Amneal NY, Amneal Ireland, and Amneal Pharma to seek approval from FDA to market and sell the Amneal ANDA Products in this District; (3) has engaged in regular and established business contacts with the State of New Jersey by, among other things, contracting and engaging in related commercial activities related to the marketing, making, shipping, using, offering to sell or selling Defendants' products in this District, and deriving substantial revenue from such activities; and (4) has made agreements with retailers, wholesalers

or distributors providing for the distribution of Defendants' products in the State of New Jersey.

ANSWER: Paragraph 40 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 40 is required, for purposes of this action only, Defendants do not contest venue in this District. Otherwise denied.

41. On information and belief, Defendant Amneal Pharma has a regular and established place of business in this District at least because it: (1) has a principal place of business in the State of New Jersey; (2) has acted in concert with Amneal NY, Amneal Ireland, and Amneal Inc. to seek approval from FDA to market and sell the Amneal ANDA Products in this District; (3) has engaged in regular and established business contacts with the State of New Jersey by, among other things, contracting and engaging in related commercial activities related to the marketing, making, shipping, using, offering to sell or selling Defendants' products in this District, and deriving substantial revenue from such activities; and (4) has made agreements with retailers, wholesalers or distributors providing for the distribution of Defendants' products in the State of New Jersey.

ANSWER: Paragraph 41 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 41 is required, for purposes of this action only, Defendants do not contest venue in this District. Otherwise denied.

42. On information and belief, Defendant Amneal NY has a regular and established place of business in this District at least because it: (1) has a principal place of business in the State of New Jersey; (2) has acted in concert with Amneal Ireland, Amneal Pharma, and Amneal Inc. to seek approval from FDA to market and sell the Amneal ANDA Products in this District; (3) has engaged in regular and established business contacts with the State of New Jersey by, among other things, contracting and engaging in related commercial activities related to the marketing, making, shipping, using, offering to sell or selling Defendants' products in this District, and deriving

substantial revenue from such activities; and (4) has made agreements with retailers, wholesalers or distributors providing for the distribution of Defendants' products in the State of New Jersey.

ANSWER: Paragraph 42 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 42 is required, for purposes of this action only, Defendants do not contest venue in this District. Otherwise denied.

43. On information and belief, Defendant Amneal Ireland has a regular and established place of business in this District at least because it: (1) has acted in concert with Amneal NY, Amneal Pharma, and Amneal Inc. to seek approval from FDA to market and sell the Amneal ANDA Products in this District; (2) conducts business, individually and/or in concert with its U.S. agent, Amneal NY that is located in the State of New Jersey, in this District; and (3) has engaged in regular and established business contacts with the State of New Jersey by, among other things, marketing, making, shipping, using, offering to sell or selling Defendants' products in this District, and deriving substantial revenue from such activities.

ANSWER: Paragraph 43 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 43 is required, for purposes of this action only, Defendants do not contest venue in this District. Otherwise denied.

44. Venue is also proper in this District for Amneal Ireland at least because, among other things, Amneal Ireland is a foreign corporation organized and existing under the laws of Ireland and may be sued in any judicial district in which it is subject to personal jurisdiction, including in the State of New Jersey. *See* 28 U.S.C. § 1391(c)(3); *see also* 28 U.S.C. § 1400(b).

ANSWER: Paragraph 44 contains legal conclusions to which no answer is required. To the extent an answer to paragraph 44 is required, for purposes of this action only, Defendants do not contest venue in this District. Otherwise denied.

BACKGROUND

NDA No. 021457

45. Teva Branded is the holder of New Drug Application ("NDA") No. 021457, under which FDA approved the commercial marketing of ProAir® HFA (albuterol sulfate) Inhalation Aerosol on October 29, 2004. ProAir® HFA (albuterol sulfate) Inhalation Aerosol is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.

ANSWER: On information and belief, admitted.

46. On October 1, 2022, the manufacturing of branded ProAir® HFA (albuterol sulfate) Inhalation Aerosol was discontinued. Teva USA currently distributes an authorized generic of ProAir® HFA (albuterol sulfate) Inhalation Aerosol under NDA No. 021457 in the United States.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of this allegation, and on that basis deny same.

The '712 Patent

47. The '712 patent, titled "Metered-Dose Inhaler," duly and legally issued on March 13, 2012. A true and correct copy of the '712 patent is attached hereto as Exhibit A.

ANSWER: Defendants admit that the '712 patent bears the title "Metered-Dose Inhaler." Defendants admit that the '712 patent bears an issue date of March 13, 2012. Defendants admit that there was an Exhibit A attached to the First Amended Complaint and that Exhibit A appears to be a copy of the '712 patent. Otherwise denied.

48. Norton is the owner and assignee of the '712 patent.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of this allegation, and on that basis deny same.

49. The '712 patent is listed in connection with ProAir® HFA (NDA No. 021457) in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book").

ANSWER: Admitted.

50. The Orange Book currently lists the expiration of the '712 patent as September 7, 2028.

ANSWER: Admitted.

The '289 Patent

51. The '289 patent, titled "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof," duly and legally issued on October 11, 2016. A true and correct copy of the '289 patent is attached hereto as Exhibit B.

ANSWER: Defendants admit that the '289 patent bears the title "Dose Counters for Inhalers, Inhalers and Methods of Assembly Thereof." Defendants admit that the '289 patent bears an issue date of October 11, 2016. Defendants admit that there was an Exhibit B attached to the First Amended Complaint and that Exhibit B appears to be a copy of the '289 patent. Otherwise denied.

52. Norton is the owner and assignee of the '289 patent.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of this allegation, and on that basis deny same.

53. The '289 patent is listed in connection with ProAir® HFA (NDA No. 021457) in

the Orange Book.

ANSWER: Admitted.

54. The Orange Book currently lists the expiration of the ’289 patent as May 18, 2031.

ANSWER: Admitted.

The ’587 Patent

55. The ’587 patent, titled “Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator,” duly and legally issued on November 7, 2017. A true and correct copy of the ’587 patent is attached hereto as Exhibit C.

ANSWER: Defendants admit that the ’587 patent bears the title “Dose Counters for Inhaler Having an Anti-Reverse Rotation Actuator.” Defendants admit that the ’587 patent bears an issue date of November 7, 2017. Defendants admit that there was an Exhibit C attached to the First Amended Complaint and that Exhibit C appears to be a copy of the ’587 patent. Otherwise denied.

56. Norton is the owner and assignee of the ’587 patent.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of this allegation, and on that basis deny same.

57. The ’587 patent is listed in connection with ProAir® HFA (NDA No. 021457) in the Orange Book.

ANSWER: Admitted.

58. The Orange Book currently lists the expiration of the ’587 patent as May 18, 2031.

ANSWER: Admitted.

The '808 Patent

59. The '808 patent, titled "Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator," duly and legally issued on February 18, 2020. A true and correct copy of the '808 patent is attached hereto as Exhibit D.

ANSWER: Defendants admit that the '808 patent bears the title "Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator." Defendants admit that the '808 patent bears an issue date of February 18, 2020. Defendants admit that there was an Exhibit D attached to the First Amended Complaint and that Exhibit D appears to be a copy of the '808 patent. Otherwise denied.

60. Norton is the owner and assignee of the '808 patent.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of this allegation, and on that basis deny same.

61. The '808 patent is listed in connection with ProAir® HFA (NDA No. 021457) in the Orange Book.

ANSWER: Admitted.

62. The Orange Book currently lists the expiration of the '808 patent as January 1, 2032.

ANSWER: Admitted.

The '889 Patent

63. The '889 patent, titled "Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator," duly and legally issued on July 26, 2022. A true and correct copy of the '889 patent is attached hereto as Exhibit E.

ANSWER: Defendants admit that the '889 patent bears the title "Dose Counter for Inhaler Having an Anti-Reverse Rotation Actuator." Defendants admit that the '889 patent bears an issue date of July 26, 2022. Defendants admit that there was an Exhibit E attached to the First Amended Complaint and that Exhibit E appears to be a copy of the '889 patent. Otherwise denied.

64. Norton is the owner and assignee of the '889 patent.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of this allegation, and on that basis deny same.

65. The '889 patent is listed in connection with ProAir® HFA (NDA No. 021457) in the Orange Book.

ANSWER: Admitted.

66. The Orange Book currently lists the expiration of the '889 patent as May 18, 2031.

ANSWER: Admitted.

Defendants' ANDA and Notice of Paragraph IV Certification

67. On information and belief, Defendants have submitted or caused the submission of Amneal's ANDA to FDA under 21 U.S.C. § 355(j), to obtain approval to engage in the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of the Amneal ANDA Products prior to the expiration of the Patents-in-Suit.

ANSWER: Admitted.

68. On information and belief, FDA has not yet approved Amneal's ANDA.

ANSWER: Admitted.

69. In the Amneal Notice Letter, Defendant Amneal NY notified Plaintiffs of the

submission of Amneal's ANDA to FDA.

ANSWER: Admitted.

70. In the Amneal Notice Letter, Defendant Amneal NY notified Plaintiffs that Amneal had filed a Paragraph IV Certification with respect to each of the Patents-in-Suit and was seeking approval from FDA to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the Patents-in- Suit.

ANSWER: Admitted.

71. The purpose of Defendants' submission of Amneal's ANDA to FDA was to obtain approval under the Federal Food, Drug and Cosmetic Act to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the Patents-in-Suit.

ANSWER: Admitted.

72. On information and belief, Defendants, through their own actions and through the actions of their agents, affiliates, and subsidiaries, prepared and submitted Amneal's ANDA, and intend to further prosecute Amneal's ANDA. On information and belief, if FDA approves Amneal's ANDA, Defendants will manufacture, offer for sale, or sell the Amneal ANDA Products within the United States, or will import the Amneal ANDA Products into the United States. On information and belief, if FDA approves Amneal's ANDA, Defendants, through their own actions and through the actions of their agents, affiliates, and subsidiaries, will actively induce or contribute to the manufacture, use, offer for sale, sale, or importation of the Amneal ANDA Products in or into the United States.

ANSWER: Admitted.

73. In the Amneal Notice Letter, Defendant Amneal NY stated that the subject of Amneal's ANDA is "Albuterol Sulfate Inhalation Aerosol, 90 mcg per actuation."

ANSWER: Admitted.

74. In the Amneal Notice Letter, Defendant Amneal NY stated that the active ingredient of the Amneal ANDA Products is albuterol sulfate.

ANSWER: Admitted.

75. In the Amneal Notice Letter, Defendant Amneal NY stated that the dosage form of the Amneal ANDA Products is "inhalation aerosol."

ANSWER: Admitted.

76. In the Amneal Notice Letter, Defendant Amneal NY stated that the strength of the Amneal ANDA Products is 90 mcg per actuation.

ANSWER: Admitted.

77. On information and belief, Amneal's ANDA contains a Paragraph IV Certification with respect to each of the Patents-in-Suit asserting that the Patents-in-Suit are unenforceable, invalid, and/or will not be infringed by the manufacture, use, offer for sale, sale, or importation of the Amneal ANDA Products ("Amneal's Paragraph IV Certification"). Defendants notified Plaintiffs of Amneal's Paragraph IV Certification in the Amneal Notice Letter, dated August 24, 2023, sent by United Parcel Service.

ANSWER: Admitted.

78. In the Amneal Notice Letter, Defendants offered Plaintiffs confidential access to ANDA No. 211600 on terms and conditions set forth in an attached "Offer of Confidential Access"

("OCA"). The OCA provided by Defendants contained various terms and conditions, several of which went above and beyond protections typically afforded in a protective order.

ANSWER: Defendants admit that in the Amneal Notice Letter, Defendants offered Plaintiffs confidential access to ANDA No. 211600 on terms and conditions set forth in an attached "Offer of Confidential Access" ("OCA"). Defendants admit that the OCA provided by Defendants contained various terms and conditions. Otherwise denied.

79. By correspondence, counsel for Plaintiffs and counsel for Defendants discussed the terms of Defendants' OCA.

ANSWER: Admitted.

80. On September 16, 2023, Plaintiffs' counsel sent Defendants' counsel an email identifying various unreasonably restrictive terms in Defendants' OCA. Plaintiffs' counsel also included a revised draft of the OCA in this correspondence.

ANSWER: Defendants admit that Plaintiffs' counsel sent Defendants' counsel an email on September 16, 2023 providing a revised OCA. Otherwise denied.

81. On September 25, 2023, Defendants' counsel sent Plaintiffs' counsel a revised OCA. That offer addressed some of Plaintiffs' concerns but remained unreasonably restrictive.

ANSWER: Defendants admit that Defendants' counsel sent Plaintiffs' counsel a further revised OCA on September 25, 2023. Otherwise denied.

82. On September 27, 2023, Plaintiffs' counsel sent another email reiterating its concerns regarding the restrictions in Defendants' OCA, and attaching a revised draft of the OCA.

ANSWER: Defendants admit that on September 27, 2023, Plaintiffs' counsel sent another email to Defendants' counsel attaching a further revised draft of the OCA. Otherwise denied.

83. On September 28, 2023, the parties reached agreement on the terms of the OCA, which was finalized on October 2, 2023. Amneal did not produce any portion of its ANDA until October 3, 2023 and did not produce the requested samples until October 4, 2023, shortly before the 45-day statutory deadline to file suit.

ANSWER: Defendants admit that the parties reached agreement on the terms of the OCA on September 28, 2023, that the OCA was finalized on October 2, 2023, that Defendants produced its ANDA on October 3, 2023 and produced samples on October 4, 2023. Otherwise denied.

84. The Amneal Notice Letter appends a document titled "Detailed Factual and Legal Basis of Non-Infringement, Unenforceability, and/or Invalidity" asserting that the commercial manufacture, use, offer for sale, or sale of the Amneal ANDA Products will not infringe any of the Patents-in-Suit ("Detailed Statement"). However, the Amneal Notice Letter and "Detailed Statement" do not provide information regarding the Amneal ANDA Products sufficient to evaluate Defendants' assertions of noninfringement.

ANSWER: Defendants admit that the Amneal Notice Letter appends a document titled "Detailed Factual and Legal Basis of Non-Infringement, Unenforceability, and/or Invalidity" asserting that the commercial manufacture, use, offer for sale, or sale of the Amneal ANDA Products will not infringe any of the Patents-in-Suit ("Detailed Statement"). Otherwise denied.

85. Given the 45-day statutory deadline to file suit set forth in 21 U.S.C.

§ 355(j)(5)(B)(iii), the timing of the production of Amneal's ANDA and samples, and the limited information provided by Defendants to date, Plaintiffs turn to the judicial process and the aid of discovery to obtain, under appropriate judicial safeguards, such information as is required to further confirm their allegations of infringement and to present to the Court evidence that the Amneal ANDA Products fall within the scope of one or more claims of the Patents-in-Suit.

ANSWER: Defendants deny that the purpose for which Plaintiffs "turn to the judicial process" is as stated in paragraph 85. Defendants lack information sufficient to form a belief as to remaining allegations of paragraph 85 and on that basis deny same.

86. This action was commenced within 45 days from the date of Plaintiffs' receipt of the Amneal Notice Letter.

ANSWER: Admitted.

COUNT I – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 8,132,712 UNDER 35 U.S.C. § 271(E)(2)

87. Plaintiffs incorporate each of the preceding paragraphs 1–86 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–86 as if fully set forth herein.

88. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '712 patent was an act of infringement of the '712 patent under 35 U.S.C. § 271(e)(2)(A).

ANSWER: Denied.

89. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '712 patent under 35 U.S.C. § 271(a)-(c).

ANSWER: Denied.

90. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '712 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

91. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '712 patent.

ANSWER: Denied.

92. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 92, and deny them on that basis.

93. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '712 patent, including at least claim 1.

ANSWER: Denied.

94. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '712 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

95. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '712 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '712 patent after approval of Amneal's ANDA.

ANSWER: Denied.

96. The foregoing actions by Amneal constitute and/or will constitute infringement of the '712 patent, active inducement of infringement of the '712 patent, and contribution to the infringement by others of the '712 patent.

ANSWER: Denied.

97. On information and belief, Amneal has acted with full knowledge of the '712 patent and without a reasonable basis for believing that it would not be liable for infringing the '712 patent, actively inducing infringement of the '712 patent, and contributing to the infringement by others of the '712 patent.

ANSWER: Denied.

98. Unless Amneal is enjoined from infringing the '712 patent, actively inducing infringement of the '712 patent, and contributing to the infringement by others of the '712 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT II – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 8,132,712

99. Plaintiffs incorporate each of the preceding paragraphs 1–98 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–98 as if fully set forth herein.

100. Amneal has knowledge of the '712 patent.

ANSWER: Admitted.

101. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '712 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

102. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 102, and deny them on that basis.

103. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '712 patent, including at least claim 1.

ANSWER: Denied.

104. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '712 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

105. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '712 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '712 patent after approval of Amneal's ANDA.

ANSWER: Denied.

106. The foregoing actions by Amneal constitute and/or will constitute infringement of the '712 patent, active inducement of infringement of the '712 patent, and contribution to the infringement by others of the '712 patent.

ANSWER: Denied.

107. On information and belief, Amneal has acted with full knowledge of the '712 patent and without a reasonable basis for believing that it would not be liable for infringing the '712 patent, actively inducing infringement of the '712 patent, and contributing to the infringement by others of the '712 patent.

ANSWER: Denied.

108. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling

according to Amneal's ANDA will infringe one or more claims of the '712 patent, including at least claim 1, and whether said claims of the '712 patent are valid.

ANSWER: Denied.

109. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '712 patent and that the claims of the '712 patent are valid.

ANSWER: Denied.

110. Amneal should be enjoined from infringing the '712 patent, actively inducing infringement of the '712 patent, and contributing to the infringement by others of the '712 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT III – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 9,463,289 UNDER 35 U.S.C. § 271(E)(2)

111. Plaintiffs incorporate each of the preceding paragraphs 1–110 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–110 as if fully set forth herein.

112. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '289 patent was an act of infringement of the '289 patent under 35 U.S.C. § 271(e)(2)(A).

ANSWER: Denied.

113. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '289 patent under 35 U.S.C. § 271(a)-(c).

ANSWER: Denied.

114. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '289 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

115. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '289 patent.

ANSWER: Denied.

116. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 116, and deny them on that basis.

117. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '289 patent, including at least claim 1.

ANSWER: Denied.

118. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '289 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

119. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '289 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '289 patent after approval of Amneal's ANDA.

ANSWER: Denied.

120. The foregoing actions by Amneal constitute and/or will constitute infringement of the '289 patent, active inducement of infringement of the '289 patent, and contribution to the infringement by others of the '289 patent.

ANSWER: Denied.

121. On information and belief, Amneal has acted with full knowledge of the '289 patent and without a reasonable basis for believing that it would not be liable for infringing the '289 patent, actively inducing infringement of the '289 patent, and contributing to the infringement by others of the '289 patent.

ANSWER: Denied.

122. Unless Amneal is enjoined from infringing the '289 patent, actively inducing

infringement of the ’289 patent, and contributing to the infringement by others of the ’289 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT IV – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 9,463,289

123. Plaintiffs incorporate each of the preceding paragraphs 1–122 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–122 as if fully set forth herein.

124. Amneal has knowledge of the ’289 patent.

ANSWER: Admitted.

125. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the ’289 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

126. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal’s ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 126, and deny them on that basis.

127. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal’s proposed labeling for those products would infringe one or more

claims of the ’289 patent, including at least claim 1.

ANSWER: Denied.

128. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the ’289 patent when Amneal’s ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

129. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the ’289 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the ’289 patent after approval of Amneal’s ANDA.

ANSWER: Denied.

130. The foregoing actions by Amneal constitute and/or will constitute infringement of the ’289 patent, active inducement of infringement of the ’289 patent, and contribution to the infringement by others of the ’289 patent.

ANSWER: Denied.

131. On information and belief, Amneal has acted with full knowledge of the ’289 patent and without a reasonable basis for believing that it would not be liable for infringing the ’289 patent, actively inducing infringement of the ’289 patent, and contributing to the infringement by others of the ’289 patent.

ANSWER: Denied.

132. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '289 patent, including at least claim 1, and whether said claims of the '289 patent are valid.

ANSWER: Denied.

133. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '289 patent and that the claims of the '289 patent are valid.

ANSWER: Denied.

134. Amneal should be enjoined from infringing the '289 patent, actively inducing infringement of the '289 patent, and contributing to the infringement by others of the '289 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT V – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 9,808,587 UNDER 35 U.S.C. § 271(E)(2)

135. Plaintiffs incorporate each of the preceding paragraphs 1–134 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–134 as if fully set forth herein.

136. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to

engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '587 patent was an act of infringement of the '587 patent under 35 U.S.C. § 271(e)(2)(A).

ANSWER: Denied.

137. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '587 patent under 35 U.S.C. § 271(a)-(c).

ANSWER: Denied.

138. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '587 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

139. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '587 patent.

ANSWER: Denied.

140. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 140, and deny them on that basis.

141. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '587 patent, including at least claim 1.

ANSWER: Denied.

142. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '587 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

143. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '587 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '587 patent after approval of Amneal's ANDA.

ANSWER: Denied.

144. The foregoing actions by Amneal constitute and/or will constitute infringement of the '587 patent, active inducement of infringement of the '587 patent, and contribution to the infringement by others of the '587 patent.

ANSWER: Denied.

145. On information and belief, Amneal has acted with full knowledge of the '587 patent and without a reasonable basis for believing that it would not be liable for infringing the '587 patent, actively inducing infringement of the '587 patent, and contributing to the infringement by others of the '587 patent.

ANSWER: Denied.

146. Unless Amneal is enjoined from infringing the '587 patent, actively inducing infringement of the '587 patent, and contributing to the infringement by others of the '587 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT VI – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 9,808,587

147. Plaintiffs incorporate each of the preceding paragraphs 1–146 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–146 as if fully set forth herein.

148. Amneal has knowledge of the '587 patent.

ANSWER: Admitted.

149. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '587 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

150. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 150, and deny them on that basis.

151. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '587 patent, including at least claim 1.

ANSWER: Denied.

152. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '587 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

153. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '587 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '587 patent after approval of Amneal's ANDA.

ANSWER: Denied.

154. The foregoing actions by Amneal constitute and/or will constitute infringement of the '587 patent, active inducement of infringement of the '587 patent, and contribution to the infringement by others of the '587 patent.

ANSWER: Denied.

155. On information and belief, Amneal has acted with full knowledge of the '587 patent and without a reasonable basis for believing that it would not be liable for infringing the '587 patent, actively inducing infringement of the '587 patent, and contributing to the infringement by others of the '587 patent.

ANSWER: Denied.

156. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '587 patent, including at least claim 1, and whether said claims of the '587 patent are valid.

ANSWER: Denied.

157. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '587 patent and that the claims of the '587 patent are valid.

ANSWER: Denied.

158. Amneal should be enjoined from infringing the '587 patent, actively inducing infringement of the '587 patent, and contributing to the infringement by others of the '587 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT VII – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 10,561,808 UNDER 35 U.S.C. § 271(E)(2)

159. Plaintiffs incorporate each of the preceding paragraphs 1–158 as if fully set forth herein.

ANSWER: Defendants incorporate each of the preceding paragraphs 1–158 as if fully set forth herein.

160. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '808 patent was an act of infringement of the '808 patent under 35 U.S.C. § 271(e)(2)(A).

ANSWER: Denied.

161. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '808 patent under 35 U.S.C. § 271(a)-(c).

ANSWER: Denied.

162. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '808 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

163. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '808 patent.

ANSWER: Denied.

164. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 164, and deny them on that basis.

165. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '808 patent, including at least claim 1.

ANSWER: Denied.

166. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '808 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

167. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '808 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '808 patent after approval of Amneal's ANDA.

ANSWER: Denied.

168. The foregoing actions by Amneal constitute and/or will constitute infringement of the '808 patent, active inducement of infringement of the '808 patent, and contribution to the infringement by others of the '808 patent.

ANSWER: Denied.

169. On information and belief, Amneal has acted with full knowledge of the '808 patent and without a reasonable basis for believing that it would not be liable for infringing the '808 patent, actively inducing infringement of the '808 patent, and contributing to the infringement by others of the '808 patent.

ANSWER: Denied.

170. Unless Amneal is enjoined from infringing the '808 patent, actively inducing infringement of the '808 patent, and contributing to the infringement by others of the '808 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT VIII – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 10,561,808

171. Plaintiffs incorporate each of the preceding paragraphs 1–170 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–170 as if fully set forth herein.

172. Amneal has knowledge of the '808 patent.

ANSWER: Admitted.

173. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '808 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

174. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 174, and deny them on that basis.

175. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '808 patent, including at least claim 1.

ANSWER: Denied.

176. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '808 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

177. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '808 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '808 patent after approval of Amneal's ANDA.

ANSWER: Denied.

178. The foregoing actions by Amneal constitute and/or will constitute infringement of the '808 patent, active inducement of infringement of the '808 patent, and contribution to the infringement by others of the '808 patent.

ANSWER: Denied.

179. On information and belief, Amneal has acted with full knowledge of the '808 patent and without a reasonable basis for believing that it would not be liable for infringing the '808 patent, actively inducing infringement of the '808 patent, and contributing to the infringement by others of the '808 patent.

ANSWER: Denied.

180. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '808 patent, including at least claim 1, and whether said claims of the '808 patent are valid.

ANSWER: Denied.

181. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '808 patent and that the claims of the '808 patent are valid.

ANSWER: Denied.

182. Amneal should be enjoined from infringing the '808 patent, actively inducing infringement of the '808 patent, and contributing to the infringement by others of the '808 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT IX – INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 11,395,889 UNDER 35 U.S.C. § 271(E)(2)

183. Plaintiffs incorporate each of the preceding paragraphs 1–182 as if fully set forth herein.

ANSWER: Defendants incorporate each of the preceding paragraphs 1–182 as if fully set forth herein.

184. Amneal's submission of Amneal's ANDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the '889 patent was an act of infringement of the '889 patent under 35 U.S.C. § 271(e)(2)(A).

ANSWER: Denied.

185. If approved by FDA, Amneal's commercial manufacture, use, importation, sale, and/or offer for sale of the Amneal ANDA Products in or into the United States will directly infringe, contribute to the infringement of, and/or actively induce the infringement of one or more claims of the '889 patent under 35 U.S.C. § 271(a)-(c).

ANSWER: Denied.

186. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '889 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

187. In the Amneal Notice Letter, Amneal did not contest, or otherwise assert, any grounds challenging, the validity or enforceability of any claim of the '889 patent.

ANSWER: Denied.

188. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 188, and deny them on that basis.

189. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '889 patent, including at least claim 1.

ANSWER: Denied.

190. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '889 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

191. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '889 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '889 patent after approval of Amneal's ANDA.

ANSWER: Denied.

192. The foregoing actions by Amneal constitute and/or will constitute infringement of the '889 patent, active inducement of infringement of the '889 patent, and contribution to the infringement by others of the '889 patent.

ANSWER: Denied.

193. On information and belief, Amneal has acted with full knowledge of the '889 patent and without a reasonable basis for believing that it would not be liable for infringing the '889 patent, actively inducing infringement of the '889 patent, and contributing to the infringement by others of the '889 patent.

ANSWER: Denied.

194. Unless Amneal is enjoined from infringing the '889 patent, actively inducing infringement of the '889 patent, and contributing to the infringement by others of the '889 patent, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

COUNT X – DECLARATORY JUDGMENT OF INFRINGEMENT BY AMNEAL OF U.S. PATENT NO. 11,395,889

195. Plaintiffs incorporate each of the preceding paragraphs 1–194 as if fully set forth herein.

ANSWER: Defendants incorporate their answers to each of the preceding paragraphs 1–194 as if fully set forth herein.

196. Amneal has knowledge of the '889 patent.

ANSWER: Admitted.

197. On information and belief, the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products would infringe one or more claims of the '889 patent, including at least claim 1, either literally or under the doctrine of equivalents.

ANSWER: Denied.

198. On information and belief, Amneal will engage in the manufacture, use, offer for sale, sale, marketing, distribution, and/or importation of the Amneal ANDA Products immediately and imminently upon FDA approval of Amneal's ANDA.

ANSWER: Defendants lack information sufficient to form a belief as to the truth of the allegations in paragraph 188, and deny them on that basis.

199. On information and belief, the use of the Amneal ANDA Products in accordance with and as directed by Amneal's proposed labeling for those products would infringe one or more claims of the '889 patent, including at least claim 1.

ANSWER: Denied.

200. On information and belief, Amneal plans and intends to, and will, actively induce infringement of the '889 patent when Amneal's ANDA is approved, and plans and intends to, and will, do so after approval.

ANSWER: Denied.

201. On information and belief, Amneal knows that the Amneal ANDA Products and their proposed labeling are especially made or adapted for use in infringing the '889 patent and that the Amneal ANDA Products and their proposed labeling are not suitable for substantial non-infringing use. On information and belief, Amneal plans and intends to, and will, contribute to infringement of the '889 patent after approval of Amneal's ANDA.

ANSWER: Denied.

202. The foregoing actions by Amneal constitute and/or will constitute infringement of the '889 patent, active inducement of infringement of the '889 patent, and contribution to the infringement by others of the '889 patent.

ANSWER: Denied.

203. On information and belief, Amneal has acted with full knowledge of the '889 patent and without a reasonable basis for believing that it would not be liable for infringing the '889 patent, actively inducing infringement of the '889 patent, and contributing to the infringement by others of the '889 patent.

ANSWER: Denied.

204. Accordingly, there is a real, substantial, and continuing case or controversy between Plaintiffs and Amneal regarding whether Amneal's manufacture, use, sale, offer for sale, or importation into the United States of the Amneal ANDA Products with their proposed labeling according to Amneal's ANDA will infringe one or more claims of the '889 patent, including at least claim 1, and whether said claims of the '889 patent are valid.

ANSWER: Denied.

205. Plaintiffs should be granted a declaratory judgment that the making, using, sale, offer for sale, and importation into the United States of the Amneal ANDA Products with their proposed labeling would infringe, actively induce the infringement of, and contribute to the infringement by others of the '889 patent and that the claims of the '889 patent are valid.

ANSWER: Denied.

206. Amneal should be enjoined from infringing the '889 patent, actively inducing infringement of the '889 patent, and contributing to the infringement by others of the '889 patent; otherwise, Plaintiffs will suffer irreparable injury. Plaintiffs have no adequate remedy at law.

ANSWER: Denied.

RESPONSE TO PLAINTIFFS' PRAYER FOR RELIEF

Defendants deny that Plaintiffs are entitled to the judgement or any of the relief requested in Plaintiffs' Prayer for Relief or otherwise.

AFFIRMATIVE DEFENSES

Defendants assert the following defenses without prejudice to the denials in this Answer and without admitting any allegations of the First Amended Complaint not otherwise admitted. Defendants reserve the right to assert additional defenses, at law or in equity, as they become known through further investigation and discovery. Defendants do not intend to hereby assume the burden of proof with respect to those matters as to which, pursuant to law, Plaintiffs bear the burden of proof.

FIRST AFFIRMATIVE DEFENSE
(Failure to State a Claim)

Plaintiffs have failed to state a claim upon which relief can be granted.

SECOND AFFIRMATIVE DEFENSE
(Lack of Subject Matter Jurisdiction)

The Court lacks subject matter jurisdiction.

THIRD AFFIRMATIVE DEFENSE
(Non-infringement of the '712 patent)

The filing of ANDA No. 211600 has not infringed and does not infringe any valid and enforceable claim of the '712 patent. Moreover, the manufacture, use, sale, and/or offer for sale of the proposed generic products that are the subject of ANDA No. 211600 has not and will not infringe any valid or enforceable claims of the '712 patent either directly or indirectly, either literally or under the doctrine of equivalents.

FOURTH AFFIRMATIVE DEFENSE
(Invalidity of the '712 patent)

The claims of the '712 patent are invalid and/or unenforceable for failure to comply with one or more of the requirements of Title 35, United States Code, including, without limitation, §§ 101, 102, 103, and/or 112, and obviousness-type double patenting.

FIFTH AFFIRMATIVE DEFENSE
(Non-infringement of the '289 patent)

The filing of ANDA No. 211600 has not infringed and does not infringe any valid and enforceable claim of the '289 patent. Moreover, the manufacture, use, sale, and/or offer for sale of the proposed generic products that are the subject of ANDA No. 211600 has not and will not infringe any valid or enforceable claims of the '289 patent either directly or indirectly, either literally or under the doctrine of equivalents.

SIXTH AFFIRMATIVE DEFENSE
(Invalidity of the '289 patent)

The claims of the '289 patent are invalid and/or unenforceable for failure to comply with one or more of the requirements of Title 35, United States Code, including, without limitation, §§ 101, 102, 103, and/or 112, and obviousness-type double patenting.

SEVENTH AFFIRMATIVE DEFENSE
(Non-infringement of the '587 patent)

The filing of ANDA No. 211600 has not infringed and does not infringe any valid and enforceable claim of the '587 patent. Moreover, the manufacture, use, sale, and/or offer for sale of the proposed generic products that are the subject of ANDA No. 211600 has not and will not infringe any valid or enforceable claims of the '587 patent either directly or indirectly, either literally or under the doctrine of equivalents.

EIGHTH AFFIRMATIVE DEFENSE
(Invalidity of the '587 patent)

The claims of the '587 patent are invalid and/or unenforceable for failure to comply with one or more of the requirements of Title 35, United States Code, including, without limitation, §§ 101, 102, 103, and/or 112, and obviousness-type double patenting.

NINTH AFFIRMATIVE DEFENSE
(Non-infringement of the '808 patent)

The filing of ANDA No. 211600 has not infringed and does not infringe any valid and enforceable claim of the '808 patent. Moreover, the manufacture, use, sale, and/or offer for sale of the proposed generic products that are the subject of ANDA No. 211600 has not and will not infringe any valid or enforceable claims of the '808 patent either directly or indirectly, either literally or under the doctrine of equivalents.

TENTH AFFIRMATIVE DEFENSE
(Invalidity of the '808 patent)

The claims of the '808 patent are invalid and/or unenforceable for failure to comply with one or more of the requirements of Title 35, United States Code, including, without limitation, §§ 101, 102, 103, and/or 112, and obviousness-type double patenting.

ELEVENTH AFFIRMATIVE DEFENSE
(Non-infringement of the '889 patent)

The filing of ANDA No. 211600 has not infringed and does not infringe any valid and enforceable claim of the '889 patent. Moreover, the manufacture, use, sale, and/or offer for sale of the proposed generic products that are the subject of ANDA No. 211600 has not and will not infringe any valid or enforceable claims of the '889 patent either directly or indirectly, either literally or under the doctrine of equivalents.

TWELFTH AFFIRMATIVE DEFENSE
(Invalidity of the '889 patent)

The claims of the '889 patent are invalid and/or unenforceable for failure to comply with one or more of the requirements of Title 35, United States Code, including, without limitation, §§ 101, 102, 103, and/or 112, and obviousness-type double patenting.

THIRTEENTH AFFIRMATIVE DEFENSE
(Unclean Hands)

Plaintiffs are barred from obtaining the relief they seek because Plaintiffs have unclean hands.

FOURTEENTH AFFIRMATIVE DEFENSE
(Patent Misuse)

U.S. Patent Nos. 8,132,712 ("the '712 patent"), 9,463,289 ("the '289 patent"), 9,808,587 ("the '587 patent"), 10,561,808 ("the '808 patent"), and 11,395,889 ("the '889 patent") (collectively, the "Asserted Patents") are unenforceable because Plaintiffs have engaged in misuse of the Asserted Patents by seeking to impermissibly broaden the scope of the patent grant with respect to the Asserted Patents, with anticompetitive effect.

[rest of page intentionally blank]

COUNTERCLAIMS

Pursuant to Rule 13 of the Federal Rules of Civil Procedure, Defendant/Counterclaim-Plaintiff Amneal Pharmaceuticals LLC ("Amneal"), by and through its counsel, alleges the following counterclaims against Plaintiffs/Counterclaim-Defendants Teva Branded Pharmaceutical Products R&D, Inc. ("Teva Branded"), Norton (Waterford) Ltd. ("Norton"), and Teva Pharmaceuticals USA, Inc. ("Teva USA") (collectively, "Counterclaim-Defendants") based on personal knowledge, the investigation of counsel, and information and belief.

NATURE OF THE ACTION

1. Amneal repeats and incorporates by reference each of the foregoing paragraphs 1–206 of its Answer as well as its Affirmative Defenses to the First Amended Complaint, as if fully set forth herein.

2. These counterclaims seek a declaratory judgment of non-infringement and invalidity of one or more claims of U.S. Patent Nos. 8,132,712 ("the '712 patent"), 9,463,289 ("the '289 patent"), 9,808,587 ("the '587 patent"), 10,561,808 ("the '808 patent"), and 11,395,889 ("the '889 patent") (collectively, the "Asserted Patents"); removal of the Asserted Patents from the Orange Book listing for ProAir® HFA, under 28 U.S.C. §§ 2201, 2202, and 21 U.S.C. § 355(j)(5)(C)(ii)(I); and relief from Counterclaim-Defendants' anticompetitive conduct to insulate, extend, and protect their monopoly in the market for ProAir® HFA and its generic equivalents, in violation of state and federal antitrust laws.

3. Upon information and belief, a true and correct copy of the '712 patent was attached to Plaintiff's First Amended Complaint as Exhibit A, a true and correct copy of the '289 patent was attached to Plaintiff's First Amended Complaint as Exhibit B, a true and correct copy of the '587 patent was attached to Plaintiff's First Amended Complaint as Exhibit C, a true and

correct copy of the '808 patent was attached to Plaintiff's First Amended Complaint as Exhibit D, and a true and correct copy of the '889 patent was attached to Plaintiff's First Amended Complaint as Exhibit E.

PARTIES

4. Amneal is a limited liability company organized and existing under the laws of the State of Delaware, having a principal place of business at 400 Crossing Boulevard, Third Floor, Bridgewater, New Jersey 08807.

5. Upon information and belief, Counterclaim-Defendant Teva Branded is a company organized under the laws of the State of Delaware with its principal place of business at 145 Brandywine Parkway, West Chester, Pennsylvania 19380. In addition, Teva Branded has a place of business at 400 Interpace Parkway #3, Parsippany, New Jersey 07054.

6. Upon information and belief, Counterclaim-Defendant Norton is a private limited company organized under the laws of the Republic of Ireland and having its registered office at Unit 301, IDA Industrial Park, Waterford X91 WK68, Republic of Ireland. Norton trades, *i.e.*, does business, as Ivax Pharmaceuticals Ireland and as Teva Pharmaceuticals Ireland.

7. Upon information and belief, Counterclaim-Defendant Teva USA is a company organized and existing under the laws of the State of Delaware, with a principal place of business at 400 Interpace Parkway, Parsippany, New Jersey 07054.

JURISDICTION AND VENUE

8. These counterclaims arise under the Patent Laws of the United States, 35 U.S.C. § 1 *et seq.*; the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202; and 21 U.S.C. § 355(j)(5)(C)(ii)(I). These counterclaims are also instituted under the Clayton Act, 15 U.S.C. §§ 15 and 26, to recover treble damages and the costs of suit, including a reasonable attorneys'

fee, for the injuries sustained by Amneal resulting from violations by Counterclaim-Defendants, as hereinafter alleged, of Section 2 of the Sherman Act, 15 U.S.C. § 2.

9. This Court has subject matter jurisdiction to hear these counterclaims under 28 U.S.C. §§ 1331, 1337(a), and 1338(a); 15 U.S.C. §§ 15 and 26; and under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. The Court has jurisdiction over the state law claims under 28 U.S.C. § 1367(a).

10. This Court has personal jurisdiction over Counterclaim-Defendants because, among other reasons, they subjected themselves to the jurisdiction of this Court by filing their Complaint and First Amended Complaint here.

11. Venue is proper in this judicial district under 28 U.S.C. §§ 1391 and 1400(b), and because Counterclaim-Defendants commenced this lawsuit in this venue.

12. There is an actual and justiciable controversy between the parties that is of sufficient immediacy and reality to warrant the relief sought in these counterclaims.

BACKGROUND

A. AMNEAL'S ANDA AND THE 30-MONTH STAY OF FDA APPROVAL OF AMNEAL'S ANDA THAT COUNTERCLAIM-DEFENDANTS TRIGGERED BY BRINGING THEIR BASELESS PATENT LITIGATION

13. On information and belief, Counterclaim-Defendant Teva Branded is the holder of New Drug Application ("NDA") No. 21-457 ("ProAir® NDA"), under which FDA approved the commercial marketing of ProAir® HFA (albuterol sulfate) Inhalation Aerosol.

14. On information and belief, Counterclaim-Defendants listed and maintained a listing for the Asserted Patents in the Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") in connection with NDA No. 021457.

15. The Asserted Patents do not meet the statutory requirements to be listed in the Orange Book, as they do not claim a drug, drug substance (active ingredient), drug product (formulation or composition), or a method of using a drug. *See* 21 U.S.C. § 355(b)(1)(A)(viii).

16. Amneal Pharmaceuticals of NY, LLC ("Amneal NY") and Amneal Ireland Ltd. ("Amneal Ireland") submitted Abbreviated New Drug Application ("ANDA") No. 211600 ("Amneal's ANDA") to the United States Food and Drug Administration ("FDA") seeking approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation into the United States of Albuterol Sulfate HFA Inhalation Aerosol, 90 mcg per actuation ("Amneal ANDA Products").

17. Amneal NY is a direct subsidiary of Amneal Pharmaceuticals LLC, and Amneal Ireland is an indirect subsidiary of Amneal Pharmaceuticals LLC.

18. Because Counterclaim-Defendants had improperly listed the Asserted Patents in the Orange Book, and because Amneal NY and Amneal Ireland sought approval from the FDA to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of a generic version of ProAir® HFA prior to the expiration of the Asserted Patents, Amneal NY and Amneal Ireland were required to file a Paragraph IV Certification with respect to each of the Asserted Patents. A Paragraph IV Certification certifies that a patent listed in the Orange Book is invalid or will not be infringed by the manufacture, use or sale of the ANDA product.

19. In accordance with 21 U.S.C. §355 (j)(2)(B)(iv)(II), by letter dated August 24, 2023 ("Amneal Notice Letter"), Amneal NY notified Counterclaim-Defendants that Amneal NY and Amneal Ireland had submitted to the FDA Amneal's ANDA including Paragraph IV Certifications as to each of the Asserted Patents.

20. On information and belief, Counterclaim-Defendants received the Amneal Notice Letter on August 28, 2023.

21. Counterclaim-Defendants filed this lawsuit on October 6, 2023, claiming that Amneal has infringed and will infringe the Asserted Patents by the filing of Amneal's ANDA with the FDA and/or by manufacturing, using, offering for sale, selling, marketing, distributing, and/or importing the products described in that ANDA.

22. The patent infringement claims that Counterclaim-Defendants asserted in this lawsuit against Amneal are objectively baseless. As described below, no reasonable litigant could expect to secure favorable relief against Amneal on the merits because the Amneal ANDA Products does not infringe any of the claims of the Asserted Patents, and the Asserted Patents are invalid.

23. Counterclaim-Defendants filed this lawsuit within 45 days of receiving the Amneal Notice Letter. By doing so, Counterclaim-Defendants triggered a 30-month stay of final FDA approval of Amneal's ANDA pursuant to 21 U.S.C. § 355(j)(5)(B)(iii). The 30-month stay, which is imposed only where an NDA holder files a patent infringement suit within 45 days of receiving notice of a Paragraph IV certification, is not set to expire until February 28, 2026 – long after Amneal expects, based on FDA correspondence to Amneal, being otherwise able to launch the Amneal ANDA Products.

24. But for Counterclaim-Defendants' improper listing of the Asserted Patents in the Orange Book and Counterclaim-Defendants' choice to bring baseless litigation within 45 days of receipt of the Amneal Notice Letter, there would be no 30-month stay imposed under 21 U.S.C. § 355(j)(5)(B)(iii).

25. During the time between the summer of 2024, when Amneal expects final approval, and February 28, 2026, Amneal will be deprived of the ability to launch its generic product, and consumers be deprived of the benefits of lower-priced generic competition from Amneal.

B. PATENT LISTING AND THE ORANGE BOOK

26. The Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301 et seq. ("FDCA" or "Act"), governs the manufacture, sale, and marketing of prescription pharmaceuticals in the United States.

27. Pursuant to the FDCA, any company that wishes to sell a new drug in the United States must seek FDA approval by filing an NDA with the FDA. As part of that application, the submitter of the NDA must provide the FDA with information identifying each patent "for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug" that is the subject of the NDA, and that either (I) "claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent;" or (II) "claims a method of using such drug for which approval is sought or has been granted in the application." 21 U.S.C. § 355(b)(1)(A)(viii); *Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC.*, 60 F.4th 1373, 1377 (Fed. Cir. 2023).

28. Submission of information on patents that do not meet these criteria is prohibited by law. 21 U.S.C. § 355(c)(2) ("Patent information that is not the type of patent information required by subsection (b)(1)(A)(viii) shall not be submitted under this paragraph.").

29. Upon approval of an NDA, the patent information submitted to the FDA by the NDA holder under 21 U.S.C. § 355(b)(1)(A)(viii) is published by the FDA in a publicly-available online database entitled "Approved Drug Products with Therapeutic Equivalence

Evaluations | Orange Book" (the "Orange Book"). *Jazz Pharms., Inc.*, 60 F.4th at 1377. The Orange Book is located at the following web address: https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book.

30. "[T]he FDA does not verify that submitted patents actually meet the statutory listing criteria, nor does the FDA proactively remove improperly listed patents" from the Orange Book. *Jazz Pharms., Inc.*, 60 F.4th at 1378. Rather, the FDA's role with respect to Orange Book patent listings is "purely ministerial." *Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1347 (Fed. Cir. 2003) (noting FDA arguments that (i) FDA does not have a duty to determine "whether the patent claims the drug," (ii) "FDA has a only a ministerial role in the listing process," and (iii) "it is the responsibility of the NDA holder to determine whether a patent claims the drug or a method of using the drug that is the subject of the NDA for purposes of Orange Book listing"); *Jazz Pharmaceuticals, Inc.*, 60 F.4th at 1378.

31. The FDA has adopted a regulation, 21 C.F.R. § 314.53(f), codifying and implementing its position that its duties with respect to Orange Book listings are purely ministerial. *Apotex, Inc.*, 347 F.3d at 1347. Under this regulation, a third party may dispute an Orange Book listing, but the FDA will not modify the listing unless the NDA holder itself requests the modification. 21 C.F.R. § 314.53(f); *Apotex, Inc.*, 347 F.3d at 1347.

C. APPROVAL OF GENERIC DRUGS

32. When an ANDA is submitted to the FDA seeking permission to market a generic version of an approved NDA product, if there are no patents listed in the Orange Book for the corresponding NDA product, the ANDA must include a certification that no such patent information has been filed. 21 U.S.C. § 355 (j)(2)(A)(vii)(I). This is known as a "Paragraph I Certification."

33. If, however, there are any patents listed in the Orange Book for the corresponding NDA, for each patent listed in the Orange Book for the relevant NDA product, the ANDA must include a certification for each patent stating (a) that the patent has expired (a "Paragraph II Certification"), (b) when the patent will expire (a "Paragraph III Certification"), or (c) that the patent is invalid or will not be infringed by the manufacture, use or sale of the ANDA product (a "Paragraph IV Certification" or "PIV Certification"). 21 U.S.C. §355 (j)(2)(A)(vii)(II)-(IV).

34. If the ANDA contains only Paragraph I Certification(s) and/or Paragraph II certification(s), the FDA may approve the ANDA immediately. 21 U.S.C. § 355 (j)(5)(B)(i).

35. If the ANDA contains Paragraph III Certifications and no PIV Certification, the FDA may approve the ANDA on the patent expiration date certified in the Paragraph III certification. 21 U.S.C. §355 (j)(5)(B)(ii).

36. If an ANDA contains one or more PIV Certifications, the ANDA applicant must provide notice of same to the NDA holder and owner(s) of the corresponding patent(s) and provide a "detailed statement of the factual and legal basis for the opinion that the patent is invalid or will not be infringed." 21 U.S.C. §355 (j)(2)(B)(iv)(II).

37. If an ANDA containing a PIV Certification is the first such ANDA submitted, then, subject to other requirements, it can qualify for 180 days of generic exclusivity, during which the FDA will not make effective its approval of another ANDA product that is a generic version of the same NDA product as the first-to-file ANDA. 21 U.S.C. §355 (j)(5)(B)(iv).

38. The filing of a PIV Certification is treated under the patent law as an act of technical infringement that provides the brand company an opportunity to sue. *See* 35 U.S.C. § 271(e)(2)(A). If the NDA holder brings a patent infringement suit within 45 days after it receives the notice of the PIV filing, the FDA's approval of the corresponding ANDA will

automatically be stayed for 30 months, unless the patent litigation is resolved sooner. 21 U.S.C. §355 (j)(5)(B)(iii).

39. If an infringement action is brought against an ANDA applicant in response to receiving notice of a PIV Certification, the ANDA applicant may "assert a counterclaim seeking an order requiring the [NDA] holder to correct or delete the patent information submitted by the [NDA] holder." 21 U.S.C. § 355(j)(5)(C)(ii)(I).

D. THE PROAIR® HFA NDA AND PRODUCT

40. ProAir® HFA was approved under the ProAir® NDA.

41. The ProAir® NDA was submitted by Ivax Research, Inc. ("Ivax") to the FDA on January 31, 2003.

42. The ProAir® NDA was approved by FDA on October 29, 2004.

43. Attached as Exhibit A is a copy of the FDA approval letter reflecting the submission and approval dates for the ProAir® NDA.

44. At the time of its approval on October 29, 2004, there was no approved trade name for the product that was the subject of NDA No. 21-457.

45. The trade name originally proposed for the product that was the subject of NDA No. 21-457 was Volare HFA (Albuterol Sulfate, USP) Inhalation Aerosol. The FDA did not approve of that trade name for the product that was the subject of NDA No. 21-457.

46. Attached as Exhibit B is a copy of the collection of "Administrative Documents/Correspondence" for NDA No. 21-457 published by the FDA, reflecting the originally proposed trade name on the final page.

47. Attached as Exhibit C is a copy of the labeling for NDA No. 21-457 approved on October 29, 2004.

48. The ProAir® NDA was submitted under Section 505(b)(2) of the Drug Price Competition and Patent Term Restoration Act of 1984, and relied on Proventil HFA Inhalation Aerosol as the comparator drug.

49. Attached as Exhibit D is a copy of the Medical Review from the Approval Package for the ProAir® NDA. On at least page three, it reflects the 505(b)(2) status of the ProAir® NDA and identifies Proventil HFA Inhalation Aerosol as the comparator drug.

50. The ingredients in ProAir® HFA are albuterol sulfate, propellant HFA-134a, and ethanol. The active ingredient in ProAir® HFA is albuterol sulfate. Attached as Exhibit E is a copy of the current Prescribing Information and Patient Information for ProAir® HFA.

51. As reflected in the ProAir® HFA label, albuterol sulfate was first approved by FDA more than forty years ago, in 1981. *See* Exhibit E (ProAir® HFA Prescribing Information at page 1).

52. ProAir® HFA was initially approved without a dose counter. Attached as Exhibit D is a copy of the Medical Review from the ProAir® NDA Approval Package. Page three of this exhibit, which is internal page 2 of the Division Director's Memorandum of October 29, 2004, states: "A dose counter is not included in this drug product. This will be addressed by the applicant in future submissions."

53. The Prescribing Information and Patient Information for ProAir® HFA has been amended several times since its initial approval in 2004. Attached as Exhibit F is a copy of the list published by the FDA of the Approval Dates and History, Letters, Labels, and Reviews for the ProAir® NDA.

54. On August 17, 2010, in connection with a Supplemental New Drug Application to the ProAir® NDA, the FDA approved a revised package insert and patient instructions for use in

support of an actuator approved on September 22, 2009. Attached as Exhibit G is a copy of the August 17, 2010 Supplement Approval letter from the FDA reflecting this approval.

55. The earliest approved Prescribing Information and Patient Information for ProAir® HFA reflecting the presence of a dose counter attached to the actuator is the March 2012 revision. Attached as Exhibit H is a copy of the March 2012 revision of the Prescribing Information and Patient Information for ProAir® HFA.

56. The March 2012 revision of the Prescribing Information and Patient Information for ProAir® HFA replaced the July 2010 revision. The July 2010 revision of the Prescribing Information and Patient Information for ProAir® HFA does not refer to a dose counter. Attached as Exhibit I is a copy of the July 2010 revision of the Prescribing Information and Patient Information for ProAir® HFA.

57. ProAir® HFA is approved for treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease, and for prevention of exercise-induced bronchospasm in patients 4 years of age and older.

58. On information and belief, Counterclaim-Defendants discontinued marketing ProAir® HFA in October 2022, but continue to sell an authorized generic version of the product.

E. PRIOR ANDAS FOR GENERIC PROAIR® HFA

59. Counterclaim-Defendants Teva Branded and Norton, together with Teva Respiratory, LLC and Norton Healthcare Limited, have established a pattern and practice of improperly listing device patents in the Orange Book and subsequently asserting those device patents against ANDA filers seeking to market generic versions of ProAir® HFA within 45 days of the filing of any Paragraph IV Certification thereto, thereby ensuring the ANDA applicant's approval is subject to the automatic 30-month stay.

60. On September 5, 2012, Counterclaim-Defendants Teva Branded and Norton together with Teva Respiratory, LLC and Norton Healthcare Limited, filed a lawsuit captioned *Teva Branded Pharmaceutical Products R&D, Inc., Teva Respiratory, LLC, Norton (Waterford) Limited, and Norton Healthcare Limited v. Perrigo Pharmaceuticals Co., Perrigo Co., and Catalent Pharma Solutions, LLC*, U.S. District Court for the District of Delaware, Case 1:12-cv-01101 (defendants collectively "Perrigo"). Teva asserted U.S. Patent Nos. 7,105,152 ("the '152 patent") and 7,566,445 ("the '445 patent") in their complaint against Perrigo. The '445 patent is a device patent that Teva improperly listed in the Orange Book. On information and belief, Counterclaim-Defendants Teva Branded and Norton together with Teva Respiratory, LLC and Norton Healthcare Limited filed a lawsuit against Perrigo within the 45-day period prescribed by 21 U.S.C. § 355(j)(5)(B)(iii), thereby triggering a 30-month stay of FDA approval of Perrigo's ANDA. The lawsuit was resolved by means of a stipulated dismissal on June 20, 2014.

61. On March 21, 2017, Counterclaim-Defendants Teva Branded and Norton together with Teva Respiratory, LLC and Norton Healthcare Limited, filed a lawsuit captioned *Teva Branded Pharmaceutical Products R&D, Inc., Teva Respiratory, LLC, Norton (Waterford) Limited, and Norton Healthcare Limited v. Lupin Atlantis Holdings SA, Lupin Pharmaceuticals, Inc., and Lupin Ltd.*, U.S. District Court for the District of Delaware, Case 1:17-cv-00307 (defendants collectively "Lupin"). Teva asserted U.S. Patent Nos. 7,105,152 ("the '152 patent"), 8,132,712 ("the '712 patent"), and 9,463,289 ("the '289 patent") in the complaint against Lupin. The '712 and '289 patents are device patents that Teva improperly listed in the Orange Book, and that Counterclaim-Defendants asserted in the First Amended Complaint against Amneal in the present case. On information and belief, Counterclaim-Defendants Teva Branded and Norton together with Teva Respiratory, LLC and Norton Healthcare Limited filed their

lawsuit within the 45-day period prescribed by 21 U.S.C. § 355(j)(5)(B)(iii), thereby triggering a 30-month stay of FDA approval of Lupin's ANDA. This lawsuit against Lupin was resolved by means of a stipulated dismissal on November 2, 2017.

62. These two prior lawsuits demonstrate that Counterclaim-Defendants Teva Branded and Norton, together with Teva Respiratory, LLC and Norton Healthcare Limited, have engaged in enforcement efforts relating to device patents listed improperly in the Orange Book for ProAir® HFA to try to delay or stop generic market entry.

63. According to the FDA, the date of first commercial marketing of a generic version of ProAir® HFA by the first-to-file ANDA applicant was February 26, 2020. Attached as Exhibit J is a copy of the Paragraph IV Patent Certifications published by the FDA and dated October 16, 2023. Page two of that document contains the entry for ProAir® HFA and reflects the February 26, 2020 launch date of the first-to-file generic version of ProAir® HFA.

64. More than 180 days have elapsed since February 26, 2020.

65. Currently, there is no ANDA applicant eligible for 180-day generic exclusivity, and any such exclusivity that may once have existed has expired or has been extinguished. Accordingly, there is no barrier to removal of the Asserted Patents from the Orange Book pursuant to 21 C.F.R. § 314.53(f)(2)(i).

F. THE ORANGE BOOK LISTING FOR PROAIR® HFA AND COUNTERCLAIM-DEFENDANTS' REFUSAL TO COMPLY WITH THE FEDERAL TRADE COMMISSION'S DELISTING REQUEST

66. At the time Amneal NY and Amneal Ireland submitted Amneal's ANDA seeking FDA approval to market a generic version of ProAir® HFA, all five Asserted Patents were listed in the Orange Book for ProAir® HFA. Attached as Exhibit K is a copy of the Orange Book listing for ProAir® HFA.

67. At the time of filing this Answer, Affirmative Defenses, and Counterclaims, all five Asserted Patents remained listed in the Orange Book for ProAir®.

68. None of the Asserted Patents is properly listed in the Orange Book because all of the Asserted Patents claim devices, and none of the Asserted Patents claim a drug, drug substance (active ingredient), drug product (formulation or composition), or a method of using a drug, as required under 21 U.S.C. § 355(b)(1)(A)(viii).

69. The United States Federal Trade Commission (the "FTC") has determined that the Asserted Patents are not properly listed in the Orange Book for ProAir® HFA. On or about November 7, 2023, the FTC sent a letter (the "FTC Delisting Letter") to Counterclaim-Defendant Teva Branded informing Teva Branded that the FTC believes that all of the Asserted Patents (plus others) are "improperly or inaccurately listed in the Orange Book" for ProAir® HFA. The FTC Delisting Letter indicates that the FTC has "submitted patent listing dispute communications to the FDA" regarding all five Asserted Patents. A copy of the FTC Delisting Letter is attached hereto as Exhibit L.

70. The FTC Delisting Letter cites the FTC's September 14, 2023 statement concerning brand drug manufacturer's improper listing of patents in the Orange Book, which explains the FTC's position that patents, including the Asserted Patents, are not properly listed in the Orange Book, and that the improper listing of patents in the Orange Book "undermines the competitive process" and "may also constitute illegal monopolization . . . ."

71. In an interview published on November 12, 2023 in Citeline Regulatory's "Pink Sheet," (attached hereto as Exhibit M) Rahul Rao, the Deputy Director of the FTC's Bureau of Competition, explained why the FTC sent the FTC Delisting Letter to Teva Branded (among others):

> The Orange Book is only supposed to list patents covering active drug ingredients. So, we focused on device patents that have nothing to do with the active drug. Our staff analyzed several different types of these products and listings with an initial focus on products that were widely used and have been around for a while and we would have expected to see more generic competition. For example, asthma and COPD inhalers were a particular area of focus for us. Over 40 million Americans rely on inhalers and a lot of the drugs using these inhalers have been around for several decades. But we're still seeing people paying hundreds and hundreds of dollars for them.
>
> And we're not seeing a lot of lower cost generic use, even though the drugs have been around for several decades and have long expired drug substance patents. So that's what made inhalers like the asthma and COPD products a particular concern.
>
> * * * * *
>
> In the last few years, there's been a lot of discussion in this space on the Orange Book and how abusive listings can negatively affect competition and ultimately patients. So, we just thought more can be done here to help ensure that drug manufacturers don't abuse the Orange Book process.

72. The FTC further explained in that interview that the FTC wants Teva Branded to delist the Asserted Patents (among others):

> Q: What's your goal with the letters? Do you want companies to delist the patents? Is FTC looking to take enforcement action if they don't?
>
> Yes, we would like the companies to delist patents. We've just identified patents that we think are improperly listed and we have opted in these instances to go through the FDA process on how to address improper Orange Book listings, which involves delisting.

73. The FTC further explained in that interview that drug-device patents that do not claim the active ingredient should not be listed in the Orange Book:

> Q: …Does the FTC think that there are device patents that that can be listed or do you think that under the statute none of them can be listed?
>
> I don't think it's particularly controversial in terms of the statute, the regulations and the cases, and I think there have been FTC and FDA statements on this, that only patents that claim the active ingredient should be listed in the Orange Book. And drug-device patents that do not claim the active ingredient should not be listed.

74. The publication of that interview concludes with the following statement from the FTC:

> And ultimately, we think the law is actually relatively clear. There's not a lot of ambiguity here in terms of what should and should not be listed.

75. On information and belief, despite receiving the FTC's Delisting Letter and despite receiving notification from the FDA regarding the FTC's listing dispute regarding ProAir® HFA, none of the Counterclaim-Defendants has agreed to request that the FDA delist the Asserted Patents or requested the FDA delist the Asserted Patents.

76. None of the Asserted Patents satisfies any of the statutory requirements for being properly listed in the Orange Book.

77. None of the Asserted Patents claims a method of using a drug.

78. None of the Asserted Patents claims an approved method of using ProAir® HFA.

79. None of the Asserted Patents claims "the drug for which the applicant submitted" the ProAir® NDA.

80. None of the Asserted Patents is "a drug substance (active ingredient) patent" or claim a drug substance or active ingredient.

81. None of the Asserted Patents is "a drug product (formulation or composition) patent" or claim a drug product or drug formulation, or drug composition.

82. None of the Asserted Patents claims the active ingredient in ProAir® HFA.

83. None of the Asserted Patents claims a drug.

84. None of the Asserted Patents contains the phrase "albuterol sulfate," which is the name of the active ingredient in ProAir® HFA.

85. None of the Asserted Patents contains the word "albuterol."

86. In addition to being listed in the Orange Book for ProAir® HFA, each Asserted Patent is also concurrently listed in the Orange Book for at least one other product. Those other products include QVAR 40, QVAR 80, QVAR Redihaler, ProAir Digihaler, ProAir Respiclick, ArmonAir Digihaler, ArmonAir Respiclick, AirDuo Digihaler, and/or AirDuo Respiclick.

87. Attached as Exhibit N is a copy of the Orange Book listing for QVAR 40, which was approved under NDA No. 020911. The active ingredient in QVAR 40 is beclomethasone dipropionate.

88. Attached as Exhibit O is a copy of the Orange Book listing for QVAR 80, which was approved under NDA No. 020911. The active ingredient in QVAR 80 is beclomethasone dipropionate.

89. Attached as Exhibit P is a copy of the Orange Book listing for QVAR Redihaler, which was approved under NDA No 207921. The active ingredient in QVAR Redihaler is beclomethasone dipropionate.

90. Beclomethasone dipropionate is a different active ingredient than albuterol sulfate.

91. Attached as Exhibit Q is a copy of the Orange Book listing for ProAir Digihaler, which was approved under NDA No. 205636. The active ingredient in ProAir Digihaler is albuterol sulfate.

92. Attached as Exhibit R is a copy of the Orange Book listing for ProAir Respiclick, which was approved under NDA No. 205636. The active ingredient in ProAir Respiclick is albuterol sulfate.

93. Attached as Exhibit S is a copy of the Orange Book listing for ArmonAir Respiclick, which was approved under NDA No. 208798. The active ingredient in ArmonAir Respiclick is fluticasone propionate.

94. Attached as Exhibit T is a copy of the Orange Book listing for ArmonAir Digihaler, which was approved under NDA No. 208798. The active ingredient in ArmonAir Digihaler is fluticasone propionate.

95. Fluticasone propionate is a different active ingredient than albuterol sulfate.

96. Attached as Exhibit U is a copy of the Orange Book listing for AirDuo Digihaler, which was approved under NDA No. 208799. The active ingredients in AirDuo Digihaler are fluticasone propionate and salmeterol xinafoate.

97. Attached as Exhibit V is a copy of the Orange Book listing for AirDuo Respiclick, which was approved under NDA No. 208799. The active ingredients in AirDuo Respiclick are fluticasone propionate and salmeterol xinafoate.

98. Fluticasone propionate and salmeterol xinafoate are each a different active ingredient than albuterol sulfate.

99. The Orange Book listing of the Asserted Patents for other products shows a pattern and practice by Counterclaim-Defendants of improperly listing the Asserted Patents in the Orange Book for multiple products including ProAir® HFA to, among other things, deter generic market entry.

100. Counterclaim-Defendants' enforcement efforts against, for example, Perrigo and Lupin regarding Orange Book patents listed for ProAir® HFA further shows that Counterclaim-Defendants are using improperly-listed Orange Book patents to hinder and delay generic market entry.

G. COUNTERCLAIM-DEFENDANTS ABUSE ORANGE BOOK AND REGULATORY PROCESS BY PURSUING BASELESS PATENT LITIGATION

101. Because Counterclaim-Defendants had improperly listed the Asserted Patents in the Orange Book, Amneal NY and Amneal Ireland were required to submit Paragraph IV Certifications as to each of the Asserted Patents (rather than a Paragraph I Certification) in order to seek approval from the FDA to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of the Amneal ANDA Products prior to the expiration of the Asserted Patents. The Amneal Notice Letter, dated August 24, 2023, and, on information and belief, received by Counterclaim-Defendants on August 28, 2023, notified Counterclaim-Defendants that Amneal NY and Amneal Ireland had submitted to the FDA Amneal's ANDA including Paragraph IV Certifications as to each of the Asserted Patents.

102. In response, Counterclaim-Defendants filed this lawsuit under 35 U.S.C. § 271(e), alleging Amneal infringed the Asserted Patents. The lawsuit triggered the Hatch-Waxman Act's 30-month stay of final approval of Amneal's ANDA, which occurs only when an NDA holder files suit within 45 days of receiving notice of an ANDA with a Paragraph IV Certification. *See*

21 U.S.C. § 355(j)(5)(B)(iii). But for Counterclaim-Defendants' improper Orange Book listing, Amneal NY and Amneal Ireland would not have submitted Paragraph IV Certifications (but instead a Paragraph I Certification), and no 30-month stay would be imposed. Similarly, but for Counterclaim-Defendants' decision to file this baseless lawsuit within 45 days of receipt of the Amneal Notice Letter, no 30-month stay would be imposed.

103. Counterclaim-Defendants' patent infringement claims asserted in this lawsuit against Amneal are objectively baseless and were brought in bad faith. No reasonable litigant could expect to secure favorable relief against Amneal on the merits because Amneal's ANDA Product does not infringe any of the claims of the Asserted Patents, and the Asserted Patents are invalid.

104. Specifically, the Asserted Patents are directed to devices or portions of devices, and the device that Amneal seeks approval to use in Amneal's ANDA is itself prior art to the Asserted Patents. Thus, the Asserted Patents cannot cover the device used by Amneal under the doctrine of equivalents, because that would necessarily ensnare the prior art. And if the Amneal device is deemed to literally infringe the Asserted Patents, then axiomatically, the Asserted Patents would be invalid as anticipated.

105. Counterclaim-Defendants' patent litigation against Amneal as to the Asserted Patents constitutes sham litigation because the litigation was brought without any reasonable chance of prevailing and, on information and belief, for the specific and purpose of restricting competition by Amneal by delaying approval of Amneal's generic equivalent of ProAir® HFA.

H. MARKET POWER AND MARKET DEFINITION

106. At all relevant times, Counterclaim-Defendants had monopoly power in the market for ProAir® HFA and its generic equivalents because it had the power to raise or maintain the price of ProAir® HFA and/or an authorized generic version of ProAir® HFA

("ProAir® AG"), which Counterclaim-Defendants also marketed, at supracompetitive levels without losing enough sales to make supracompetitive prices unprofitable, as well as the power to exclude competitors.

107. At all times during Counterclaim-Defendants' monopoly, a small but significant, non-transitory increase to the price of ProAir® HFA and its generic equivalents would not have caused Counterclaim-Defendants to suffer a significant loss of sales.

108. On information and belief, ProAir® HFA and its generic equivalents do not exhibit significant, positive cross-elasticity of demand with respect to price with any other albuterol sulfate inhalant products. Notwithstanding the commercialization of other albuterol sulfate inhalant products, Counterclaim-Defendants continued to charge supracompetitive prices and exclude competitors.

109. On information and belief, Counterclaim-Defendants sold ProAir® HFA and the ProAir® AG at prices well in excess of marginal costs, and in excess of the competitive price, and enjoyed high profit margins.

110. Counterclaim-Defendants have, and have exercised, the power to exclude competition to ProAir® HFA and its generic equivalents.

111. Counterclaim-Defendants enjoyed high barriers to entry with respect to the brand and generic versions of ProAir® HFA.

112. As set out above, Counterclaim-Defendants' anticompetitive conduct—including their improper listing of the Asserted Patents in the Orange Book and their filing of this sham litigation within 45 days of the receipt of Amneal's Notice Letter—is part of a pattern of conduct that began long before the instant litigation. Counterclaim-Defendants have, and have maintained, market power throughout the entirety of the course of their anticompetitive conduct.

113. There is direct evidence of market power and anticompetitive effects available in this case sufficient to show Counterclaim-Defendants' ability to control prices of its ProAir® HFA and ProAir® AG, and to exclude relevant competitors, without the need to show the relevant antitrust markets. The direct evidence consists of, among other things, (a) the fact that additional competing generic equivalents would have entered the market at substantial discounts to the brand version but for Counterclaim-Defendants' anticompetitive conduct; (b) Counterclaim-Defendants' history of improperly listing patents in the Orange Book and filing sham litigation with respect to the same; and (c) Counterclaim-Defendants' supracompetitive pricing for ProAir® HFA and ProAir® AG.

114. To the extent proof of monopoly power by defining a relevant product market is required, Amneal alleges that the relevant antitrust market is the market for ProAir® HFA and its generic equivalents. ProAir® HFA and its generic equivalents are not reasonably interchangeable with other products due to the distinct qualities and characteristics of ProAir® HFA, which distinguish it from other albuterol sulfate inhalants. Indeed, researchers have recognized significant differences across the spectrum of albuterol sulfate HFA inhalation aerosol products. Johnson et al., *The effect of a holding chamber on albuterol metered-dose inhaler product differences*, ANNALS OF ALLERGY, ASTHMA, & IMMUNOLOGY 117(3):246-50 (2016). doi: 10.1016/j.anai.2016.07.016. PMID: 27613457 (attached as Exhibit W). Accordingly, ProAir® HFA and its generic equivalents are appropriately considered as a market of their own.

115. The United States, the District of Columbia, and the U.S. territories constitute the relevant geographic market.

116. Thus, for purposes of this lawsuit, the market for the sale of ProAir® HFA and its generic equivalents in the United States (the "Relevant Market") constitutes a relevant market. In the alternative, the relevant market encompasses all albuterol sulfate HFA inhaler aerosol products (the "Alternative Relevant Market").[1]

117. Upon information and belief, at all relevant times Counterclaim Defendants had a predominant share of the Relevant Market.

118. On information and belief, Counterclaim-Defendants were able to set prices of ProAir® HFA and the ProAir® AG above that which would be charged in a competitive market.

119. Counterclaim-Defendants possess monopoly power in the Relevant Market, as evidenced by, among other factors, their prior pricing actions and dominant market share.

I. ANTITRUST IMPACT AND IMPACT ON INTERSTATE COMMERCE

120. Amneal plans to launch the Amneal ANDA Products within days or weeks of receipt of final FDA approval.

121. Via a letter dated November 9, 2023, the FDA informed Amneal that it has set a goal date of June 25, 2024 for review of Amneal's ANDA if an inspection is not required, and a goal date of August 25, 2024 for review of Amneal's ANDA if an inspection is required. Attached as Exhibit X is a copy of the November 9, 2023 FDA letter. Amneal reasonably expects to receive FDA approval in the summer of 2024. Because of Counterclaim-Defendants anticompetitive conduct, that approval will be tentative, meaning that Amneal will need to wait until expiration of the 30-month stay to receive final approval and launch the Amneal ANDA

[1] Amneal maintains that the relevant product market for purposes of its Counterclaims is ProAir® HFA and its generic equivalents. However, to the extent the relevant product market is construed to encompass all albuterol sulfate HFA inhaler aerosol products (the Alternative Relevant Market), use of the term 'Relevant Market' herein encompasses both the Relevant Market and the Alternative Relevant Market.

Products. The approval in the summer of 2024 would be final but for Counterclaim-Defendants' anticompetitive conduct.

122. Amneal is making multi-million dollar investments to enable a successful launch as early as the summer of 2024. Specifically, in 2023 and early 2024, Amneal is making several million dollars in capital expenditures on new and expanded filling and packaging lines for the Amneal ANDA Products, as is spending several million dollars on device components, such as valves and actuators.

123. On information and belief, some of the device components that Amneal is purchasing will expire before expiration of the 30-month stay.

124. Counterclaim-Defendants' supracompetitive scheme to maintain its monopoly in the Relevant Market included delaying Amneal's entry through (1) Orange Book abuse and (2) engaging in sham litigation. Counterclaim-Defendants' anticompetitive scheme has had a direct, substantial, and adverse effect on Amneal and interstate competition in the Relevant Market by maintaining monopoly power, increasing prices, artificially creating barriers to entry, and delaying competition in the Relevant Market.

125. By impeding competition from generic equivalent products, including Amneal's, Counterclaim-Defendants' anticompetitive scheme has allowed (and, unless restrained by this Court, will continue to allow) Counterclaim-Defendants to maintain and extend their monopoly power in the Relevant Market and to sell ProAir® HFA and the ProAir® AG at artificially-inflated monopoly prices.

126. Counterclaim-Defendants' anticompetitive scheme has harmed the competitive process and has had a substantial effect on interstate commerce, as it has allowed Counterclaim Defendants to charge wholesalers, retailers, payors, and consumers nationwide supracompetitive

prices. But for this anticompetitive conduct, consumers and payors would have enjoyed the benefits of lower-priced generic competition from Amneal earlier. Instead, as a result of Counterclaim-Defendants' strategies, which include improper listing of the Asserted Patents in the Orange Book and engaging in sham litigation, consumers and payors have been forced to pay monopoly prices for Counterclaim-Defendants' ProAir® HFA and the ProAir® AG. The impact of Counterclaim-Defendants' anticompetitive conduct, and the accompanying supracompetitive pricing, is felt throughout the health care industry, impacting pharmaceutical competitors, healthcare providers, insurers, and other direct purchasers, intermediaries, and consumers.

127. Amneal has suffered, and will continue to suffer, harm as a result of Counterclaim-Defendants' anticompetitive conduct. That harm includes:

a. Loss of future sales and profits due to being foreclosed from selling in the Relevant Market;
b. The large amount of time and expense associated with having to fight baseless, sham patent litigation based on patents that were improperly listed in the Orange Book;
c. A delay in Amneal's ability to recoup its investment in filling and packaging lines and device components for the Amneal ANDA Products; and
d. The loss of Amneal's investment in device components that will expire before expiration of the 30-month stay resultant from Counterclaim-Defendants' improper listing of patents in the Orange Book.

128. A claimant satisfies the injury-in-fact requirement of standing where, as here, "the threatened injury is real, immediate, and direct." *See Pfizer Inc. v. Apotex Inc.*, 726 F. Supp. 2d 921, 930 (N.D. Ill. 2010) (quoting *Davis v. Fed. Election Com'n*, 554 U.S. 724, 734 (2008)).

129. "[T]he creation of 'an independent barrier to the drug market' by a brand drug company 'that deprives [the generic company] of an economic opportunity to compete' satisfies the injury-in-fact and causation requirements of Article III standing." *See Pfizer Inc.*, 726 F. Supp 2d at 930 (quoting *Caraco Pharm. Labs., Ltd. v. Forest Labs., Inc.*, 527 F.3d 1278, 1285 (Fed. Cir. 2008)).

130. The injury to Amneal is immediate. Amneal is already spending time and money to litigate this baseless and sham patent litigation. Because Counterclaim-Defendants filed the instant patent suit, alleging infringement of patents improperly listed in the Orange Book, Amneal's final FDA approval is subject to the automatic 30-month stay. Based on the date which Counterclaim-Defendants filed the present lawsuit, Amneal's ANDA would not be eligible for final approval until February 28, 2026. Accordingly, from the date of Amneal's imminent tentative approval (in the summer of 2024) through February 28, 2026, 2026, Amneal's ANDA will be ineligible for final approval, and Amneal therefore will be deprived of the ability to launch its generic product, as a result of the Counterclaim-Defendants' anticompetitive conduct.

131. As a result of Counterclaim-Defendants' improper listing of the Asserted Patents and sham litigation, Amneal has already suffered and will imminently suffer the injuries outlined above.

132. Counterclaim-Defendants' anticompetitive conduct, as alleged herein, is not entitled to any qualified *Noerr-Pennington* immunity, nor is it protected by the state action doctrine or any statute of limitations.

133. There is and was no legitimate, procompetitive justification for Counterclaim-Defendants' conduct. Even if there was some conceivable and cognizable justification, Counterclaim-Defendants' conduct was not necessary to achieve such a purpose, and, in any event, any procompetitive effects would be outweighed by the scheme's anticompetitive effects on Amneal, competition, and consumers.

COUNT 1:
DECLARATORY JUDGMENT
REQUIRING DELISTING OF U.S. PATENT NO. 8,132,712

134. Amneal incorporates and re-alleges each of the foregoing paragraphs 1–133 of its Counterclaims, as if fully set forth herein.

135. Amneal hereby seeks a declaration pursuant to 21 U.S.C. § 355(j)(5)(C)(ii) ordering Counterclaim-Defendants to delete or withdraw the '712 patent from the Orange Book.

136. An actual controversy exists between Counterclaim-Defendants and Amneal over the listing of the '712 patent in the Orange Book.

137. The '712 patent is not properly listed in the Orange Book.

138. The '712 patent does not satisfy any of the statutory requirements for being listed in the Orange Book.

139. The '712 patent does not claim a method of using a drug.

140. The '712 patent does not claim an approved method of using ProAir® HFA.

141. The '712 patent does not claim "the drug for which the applicant submitted" the ProAir® NDA.

142. The '712 patent is not "a drug substance (active ingredient) patent."

143. The '712 patent does not claim a drug substance.

144. The '712 patent does not claim an active ingredient.

145. The '712 patent is not "a drug product (formulation or composition) patent."

146. The '712 patent does not claim a drug product.

147. The '712 patent does not claim a drug formulation.

148. The '712 patent does not claim a drug composition.

149. The '712 patent does not claim a drug.

150. The FTC has already determined that the '712 patent is not properly listed in the Orange Book for ProAir® HFA.

151. On or about November 7, 2023, the FTC sent a letter to Teva Branded bearing that date and informing Teva Branded that the FTC believes that the '712 patent is "improperly or inaccurately listed in the Orange Book" for ProAir® HFA. A copy of the FTC Delisting Letter to Teva Branded is attached to this Answer, Affirmative Defenses, and Counterclaims as Exhibit L.

152. The FTC Delisting Letter indicates that the FTC has "submitted patent listing dispute communications to the FDA" regarding all five Asserted Patents, including the '712 patent.

153. The '712 patent contains 19 claims, of which only claims 1, 18, and 19 are independent. A copy of the '712 patent is attached as Exhibit A to the Complaint.

154. Claim 1 of the '712 patent is directed to "[a] dose counter for a metered-dose inhaler" having several recited structural features.

155. Claim 1 of the '712 patent recites as follows:

> A dose counter for a metered-dose inhaler, the counter comprising:
>
> an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery;
>
> a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear;
>
> wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

156. Claim 18 of the ’712 patent is directed to “[t]he use of a dose counter for preventing miscounting in a metered dose inhaler,” in which the dose counter has several recited structural features.

157. Claim 18 of the ’712 patent recites as follows:

> The use of a dose counter for preventing miscounting in a metered dose inhaler, the dose counter comprising:
> an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery;
> a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear;
> wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

158. Claim 19 of the ’712 patent is directed to “[t]he use of a dose counter for preventing undercounting in a metered dose inhaler,” in which the dose counter has several recited structural features.

159. Claim 19 of the ’712 patent recites as follows:

> The use of a dose counter for preventing undercounting in a metered dose inhaler, the dose counter comprising:
> an actuator; a rotary gear; a driver for driving the rotary gear in a step-wise fashion in response to displacement of the actuator, the rotary gear comprising a wheel mounted on a spindle which wheel having a plurality of ratchet teeth around its periphery;
> a pawl to prevent reverse rotation of the rotary gear; and a display coupled to the rotary gear, the display having a visible array of incrementing integers on a surface thereof indexable by a single integer in response to each step of the step-wise rotary motion of the rotary gear;

> wherein the pawl comprises at least two ratchet teeth each for engaging with the ratchet teeth of the wheel to prevent reverse rotation of the rotary gear, the at least two ratchet teeth being radially spaced such that one of the at least two ratchet teeth of the pawl engages with the ratchet teeth of the wheel following each step of the step-wise rotary motion of the rotary gear.

160. None of the claims of the '712 patent recite a drug, a drug substance, an active ingredient, a drug product, a drug formulation, a drug composition, a method of using a drug, a method of using a drug product, a method of using a drug substance, a method of using an active pharmaceutical ingredient, a method of using a drug formulation, a method of using a drug composition, or a method of using a pharmaceutical formulation.

161. None of the claims of the '712 patent recite "albuterol," "albuterol sulfate," "propellant HFA-134a," or "ethanol."

162. The '712 patent does not recite any of the following words or phrases: "albuterol," "albuterol sulfate," "HFA-134a," "ethanol," "ingredient," "formulation," or "bronchospasm."

163. Other than reciting the name of the assignee "Ivax Pharmaceuticals Ireland," the '712 patent does not recite the words "pharmaceutical," "pharmaceuticals," "pharmacological," "pharmacy," or "pharmaceutics."

164. In addition to being listed in the Orange Book entry for ProAir® HFA, the '712 patent is listed in the Orange Book entry for QVAR Redihaler.

COUNT 2:
DECLARATORY JUDGMENT
REQUIRING DELISTING OF U.S. PATENT NO. 9,463,289

165. Amneal incorporates and re-alleges each of the foregoing paragraphs 1–164 of its Counterclaims, as if fully set forth herein.

166. Amneal hereby seeks a declaration pursuant to 21 U.S.C. § 355(j)(5)(C)(ii) ordering Counterclaim-Defendants to delete or withdraw the '289 patent from the Orange Book.

167. An actual controversy exists between Counterclaim-Defendants and Amneal over the listing of the '289 patent in the Orange Book.

168. The '289 patent is not properly listed in the Orange Book.

169. The '289 patent does not satisfy any of the statutory requirements for being listed in the Orange Book.

170. The '289 patent does not claim a method of using a drug.

171. The '289 patent does not claim an approved method of using ProAir® HFA.

172. The '289 patent does not claim "the drug for which the applicant submitted" the ProAir® NDA.

173. The '289 patent is not "a drug substance (active ingredient) patent."

174. The '289 patent does not claim a drug substance.

175. The '289 patent does not claim an active ingredient.

176. The '289 patent is not "a drug product (formulation or composition) patent."

177. The '289 patent does not claim a drug product.

178. The '289 patent does not claim a drug formulation.

179. The '289 patent does not claim a drug composition.

180. The '289 patent does not claim a drug.

181. The FTC has already determined that the '289 patent is not properly listed in the Orange Book for ProAir® HFA.

182. On or about November 7, 2023, the FTC sent a letter to Teva Branded bearing that date and informing Teva Branded that the FTC believes that the '289 patent is "improperly

or inaccurately listed in the Orange Book" for ProAir® HFA. A copy of the FTC Delisting Letter to Teva Branded is attached to this Answer, Affirmative Defenses, and Counterclaims as Exhibit L.

183. The FTC Delisting Letter indicates that the FTC has "submitted patent listing dispute communications to the FDA" regarding all five Asserted Patents, including the '289 patent.

184. The '289 patent contains 10 claims, of which only claim 1 is independent. A copy of the '289 patent is attached as Exhibit B to the Complaint.

185. Claim 1 of the '289 patent recites:

> An inhaler for metered dose inhalation, the inhaler comprising:
> a main body having a canister housing,
> a medicament canister, which is moveable relative to the canister housing and retained in a central outlet port of the canister housing arranged to mate with a canister fire stem of the medicament canister, and
> a dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of the medicament canister,
> wherein the canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall, and
> wherein the canister housing has a longitudinal axis X which passes through the center of the central outlet port,
> the inner wall canister support formation, the actuation member, and the central outlet port lying in a common plane coincident with the longitudinal axis X.

186. None of the claims of the '289 patent recite a drug, a drug substance, an active ingredient, a drug product, a drug formulation, a drug composition, a method of using a drug, a method of using a drug product, a method of using a drug substance, a method of using an active pharmaceutical ingredient, a method of using a drug formulation, a method of using a drug composition, or a method of using a pharmaceutical formulation.

187. None of the claims of the ’289 patent recite “albuterol,” “albuterol sulfate,” “propellant HFA-134a,” or “ethanol.”

188. The ’289 patent does not recite any of the following words or phrases: “albuterol,” “albuterol sulfate,” “HFA-134a,” “ethanol,” “ingredient,” “formulation,” or “bronchospasm.”

189. Other than reciting the name of the assignees and applicants “Ivax Pharmaceuticals Ireland,” and “Teva Pharmaceuticals Ireland,” the ’289 patent does not recite the words “pharmaceutical,” “pharmaceuticals,” “pharmacological,” “pharmacy,” or “pharmaceutics.”

190. In addition to being listed in the Orange Book entry for ProAir® HFA, the ’289 patent is listed in the Orange Book entries for (1) QVAR40 and (2) QVAR80.

COUNT 3:
DECLARATORY JUDGMENT
REQUIRING DELISTING OF U.S. PATENT NO. 9,808,587

191. Amneal incorporates and re-alleges each of the foregoing paragraphs 1–190 of its Counterclaims, as if fully set forth herein.

192. Amneal hereby seeks a declaration pursuant to 21 U.S.C. § 355(j)(5)(C)(ii) ordering Counterclaim-Defendants to delete or withdraw the ’587 patent from the Orange Book.

193. An actual controversy exists between Counterclaim-Defendants and Amneal over the listing of the ’587 patent in the Orange Book.

194. The ’587 patent is not properly listed in the Orange Book.

195. The ’587 patent does not satisfy any of the statutory requirements for being listed in the Orange Book.

196. The ’587 patent does not claim a method of using a drug.

197. The ’587 patent does not claim an approved method of using ProAir® HFA.

198. The ’587 patent does not claim “the drug for which the applicant submitted” the ProAir® NDA.

199. The ’587 patent is not “a drug substance (active ingredient) patent.”

200. The ’587 patent does not claim a drug substance.

201. The ’587 patent does not claim an active ingredient.

202. The ’587 patent is not “a drug product (formulation or composition) patent.”

203. The ’587 patent does not claim a drug product.

204. The ’587 patent does not claim a drug formulation.

205. The ’587 patent does not claim a drug composition.

206. The ’587 patent does not claim a drug.

207. The FTC has already determined that the ’587 patent is not properly listed in the Orange Book for ProAir® HFA.

208. On or about November 7, 2023, the FTC sent a letter to Teva Branded bearing that date and informing Teva Branded that the FTC believes that the ’587 patent is “improperly or inaccurately listed in the Orange Book” for ProAir® HFA. A copy of the FTC Delisting Letter to Teva Branded is attached to this Answer, Affirmative Defenses, and Counterclaims as Exhibit L.

209. The FTC Delisting Letter indicates that the FTC has “submitted patent listing dispute communications to the FDA” regarding all five Asserted Patents, including the ’587 patent.

210. The ’587 patent contains 22 claims, of which only claims 1, 12, and 13 are independent. A copy of the ’587 patent is attached as Exhibit C to the Complaint.

211. Claim 1 of the ’587 patent recites:

> An inhaler for metered dose inhalation, the inhaler comprising:
> a main body having a canister housing,
> a medicament canister, which is moveable relative to the canister housing and retained in a central outlet port of the canister housing arranged to mate with a canister fire stem of the medicament canister, and
> a dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of the medicament canister,
> wherein the canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall,
> wherein the canister housing has a longitudinal axis X which passes through the center of the central outlet port, and
> wherein the first inner wall canister support formation, the actuation member, and the central outlet port lie in a common plane coincident with the longitudinal axis X such that the first inner wall canister support formation protects against unwanted actuation of the dose counter by reducing rocking of the medicament canister relative to the main body of the inhaler.

212. Claim 12 of the ’587 patent recites:

> An inhaler for metered dose inhalation, the inhaler comprising:
> a main body having a canister housing,
> a medicament canister, which is moveable relative to the canister housing and retained in a central outlet port of the canister housing arranged to mate with a canister fire stem of the medicament canister, and
> a dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of the medicament canister,
> wherein the canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall,
> wherein the canister housing has a longitudinal axis X which passes through the center of the central outlet port, and
> wherein the first inner wall canister support formation, the actuation member, and the central outlet port lie in a common plane coincident with the longitudinal axis X such that the first inner wall canister support formation protects against dose count errors by reducing rocking of the medicament canister towards or away from the actuation member.

213. Claim 13 of the ’587 patent recites:

> An inhaler for metered dose inhalation, the inhaler comprising:
> a main body having a canister housing,
> a medicament canister retained in the canister housing and movable relative thereto, and a dose counter, the dose counter having an actuation member having at least a portion thereof located in the canister housing for operation by movement of the medicament canister,
> wherein the canister housing has an inner wall, and a first inner wall canister support formation extending inwardly from a main surface of the inner wall,
> wherein the canister housing has an aperture formed in the inner wall through which the portion of the actuation member extends, and
> wherein the first inner wall canister support formation extends from the main surface of the inner wall to the aperture.

214. None of the claims of the ’587 patent recite a drug, a drug substance, an active ingredient, a drug product, a drug formulation, a drug composition, a method of using a drug, a method of using a drug product, a method of using a drug substance, a method of using an active pharmaceutical ingredient, a method of using a drug formulation, a method of using a drug composition, or a method of using a pharmaceutical formulation.

215. None of the claims of the ’587 patent recite “albuterol,” “albuterol sulfate,” “propellant HFA-134a,” or “ethanol.”

216. The ’587 patent does not recite any of the following words or phrases: “albuterol,” “albuterol sulfate,” “HFA-134a,” “ethanol,” “ingredient,” “formulation,” or “bronchospasm.”

217. Other than reciting the name of the assignees and applicants “Ivax Pharmaceuticals Ireland,” and “Teva Pharmaceuticals Ireland,” the ’587 patent does not recite the words “pharmaceutical,” “pharmaceuticals,” “pharmacological,” “pharmacy,” or “pharmaceutics.”

218. In addition to being listed in the Orange Book entry for ProAir® HFA, the '587 patent is listed in the Orange Book entries for (1) QVAR40 and (2) QVAR80.

COUNT 4:
DECLARATORY JUDGMENT
REQUIRING DELISTING OF U.S. PATENT NO. 10,561,808

219. Amneal incorporates and re-alleges each of the foregoing paragraphs 1–218 of its Counterclaims, as if fully set forth herein.

220. Amneal hereby seeks a declaration pursuant to 21 U.S.C. § 355(j)(5)(C)(ii) ordering Counterclaim-Defendants to delete or withdraw the '808 patent from the Orange Book.

221. An actual controversy exists between Counterclaim-Defendants and Amneal over the listing of the '808 patent in the Orange Book.

222. The '808 patent is not properly listed in the Orange Book.

223. The '808 patent does not satisfy any of the statutory requirements for being listed in the Orange Book.

224. The '808 patent does not claim a method of using a drug.

225. The '808 patent does not claim an approved method of using ProAir® HFA.

226. The '808 patent does not claim "the drug for which the applicant submitted" the ProAir® NDA.

227. The '808 patent is not "a drug substance (active ingredient) patent."

228. The '808 patent does not claim a drug substance.

229. The '808 patent does not claim an active ingredient.

230. The '808 patent is not "a drug product (formulation or composition) patent."

231. The '808 patent does not claim a drug product.

232. The '808 patent does not claim a drug formulation.

233. The ’808 patent does not claim a drug composition.

234. The ’808 patent does not claim a drug.

235. The FTC has already determined that the ’808 patent is not properly listed in the Orange Book for ProAir® HFA.

236. On or about November 7, 2023, the FTC sent a letter to Teva Branded bearing that date and informing Teva Branded that the FTC believes that the ’808 patent is “improperly or inaccurately listed in the Orange Book” for ProAir® HFA. A copy of the FTC Delisting Letter to Teva Branded is attached to this Answer, Affirmative Defenses, and Counterclaims as Exhibit L.

237. The FTC Delisting Letter indicates that the FTC has “submitted patent listing dispute communications to the FDA” regarding all five Asserted Patents, including the ’808 patent.

238. The ’808 patent contains 29 claims, of which only claim 1 is independent. A copy of the ’808 patent is attached as Exhibit D to the Complaint.

239. Claim 1 of the ’808 patent recites:

> A dose counter for an inhaler, the dose counter having
> a counter display arranged to indicate dosage information,
> a drive system arranged to move the counter display incrementally in a first direction from a first station to a second station in response to actuation input,
> wherein a regulator is provided which is arranged to act upon the counter display at the first station to regulate motion of the counter display at the first station to incremental movements.

240. None of the claims of the ’808 patent recite a drug, a drug substance, an active ingredient, a drug product, a drug formulation, a drug composition, a method of using a drug, a method of using a drug product, a method of using a drug substance, a method of using an active

pharmaceutical ingredient, a method of using a drug formulation, a method of using a drug composition, or a method of using a pharmaceutical formulation.

241. None of the claims of the '808 patent recite "albuterol," "albuterol sulfate," "propellant HFA-134a," or "ethanol."

242. The '808 patent does not recite any of the following words or phrases: "albuterol," "albuterol sulfate," "HFA-134a," "ethanol," "ingredient," "formulation," or "bronchospasm."

243. Other than reciting the name of the assignees and applicants "Ivax Pharmaceuticals Ireland," and "Teva Pharmaceuticals Ireland," the '808 patent does not recite the words "pharmaceutical," "pharmaceuticals," "pharmacological," "pharmacy," or "pharmaceutics."

244. In addition to being listed in the Orange Book entry for ProAir® HFA, the '808 patent is listed in the Orange Book entries for (1) QVAR Redihaler, (2) AirDuo Digihaler, (3) AirDuo Respiclick, (4) ArmonAir Digihaler, (5) ArmonAir Respiclick, (6) ProAir Digihaler, (7) ProAir Respiclick, (8) QVAR40, and (9) QVAR80.

COUNT 5:
DECLARATORY JUDGMENT
REQUIRING DELISTING OF U.S. PATENT NO. 11,395,889

245. Amneal incorporates and re-alleges each of the foregoing paragraphs 1–244 of its Counterclaims, as if fully set forth herein.

246. Amneal hereby seeks a declaration pursuant to 21 U.S.C. §355(j)(5)(C)(ii) ordering Counterclaim-Defendants to delete or withdraw the '889 patent from the Orange Book.

247. An actual controversy exists between Counterclaim-Defendants and Amneal over the listing of the '889 patent in the Orange Book.

248. The ’889 patent is not properly listed in the Orange Book.

249. The ’889 patent does not satisfy any of the statutory requirements for being listed in the Orange Book.

250. The ’889 patent does not claim a method of using a drug.

251. The ’889 patent does not claim an approved method of using ProAir® HFA.

252. The ’889 patent does not claim “the drug for which the applicant submitted” the ProAir® NDA.

253. The ’889 patent is not “a drug substance (active ingredient) patent.”

254. The ’889 patent does not claim a drug substance.

255. The ’889 patent does not claim an active ingredient.

256. The ’889 patent is not “a drug product (formulation or composition) patent.”

257. The ’889 patent does not claim a drug product.

258. The ’889 patent does not claim a drug formulation.

259. The ’889 patent does not claim a drug composition.

260. The ’889 patent does not claim a drug.

261. The FTC has already determined that the ’889 patent is not properly listed in the Orange Book for ProAir® HFA.

262. On or about November 7, 2023, the FTC sent a letter to Teva Branded bearing that date and informing Teva Branded that the FTC believes that the ’889 patent is “improperly or inaccurately listed in the Orange Book” for ProAir® HFA. A copy of the FTC Delisting Letter to Teva Branded is attached to this Answer, Affirmative Defenses, and Counterclaims as Exhibit L.

263. The FTC Delisting Letter indicates that the FTC has "submitted patent listing dispute communications to the FDA" regarding all five Asserted Patents, including the '889 patent.

264. The '889 patent contains 6 claims, of which only claim 1 is independent. A copy of the '889 patent is attached as Exhibit E to the Complaint.

265. Claim 1 of the '889 patent recites:

> An incremental dose counter for a metered dose inhaler having a body arranged to retain a canister for movement of the canister relative thereto, the incremental dose counter having a main body,
>
> an actuator arranged to be driven and to drive an incremental output member in a count direction in response to canister motion, the actuator being configured to restrict motion of the output member in a direction opposite to the count direction, such that the actuator acts as an anti-back drive member when the actuator is in a non-depressed position, and
>
> wherein the incremental dose counter further comprises a second anti-back member configured to restrict motion of the output member in a direction opposite to the count direction when the actuator is disengaged from the output member by a bump surface.

266. None of the claims of the '889 patent recite a drug, a drug substance, an active ingredient, a drug product, a drug formulation, a drug composition, a method of using a drug, a method of using a drug product, a method of using a drug substance, a method of using an active pharmaceutical ingredient, a method of using a drug formulation, a method of using a drug composition, or a method of using a pharmaceutical formulation.

267. None of the claims of the '889 patent recite "albuterol," "albuterol sulfate," "propellant HFA-134a," or "ethanol."

268. The '889 patent does not recite any of the following words or phrases: "albuterol," "albuterol sulfate," "HFA-134a," "ethanol," "ingredient," "formulation," or "bronchospasm."

269. Other than reciting the name of the assignees and applicants "Ivax Pharmaceuticals Ireland," and "Teva Pharmaceuticals Ireland," the '889 patent does not recite the words "pharmaceutical," "pharmaceuticals," "pharmacological," "pharmacy," or "pharmaceutics."

270. In addition to being listed in the Orange Book entry for ProAir® HFA, the '889 patent is listed in the Orange Book entries for (1) QVAR Redihaler, (2) QVAR40, and (3) QVAR80.

COUNT 6:
UNLAWFUL MONOPOLIZATION – OVERALL SCHEME
IN VIOLATION OF THE SHERMAN ACT

271. Amneal incorporates and re-alleges each of the foregoing paragraphs 1–270 of its Counterclaims, as if fully set forth herein.

272. This claim arises under the Sherman Act, 15 U.S.C. § 2 and under the Clayton Act, 15 U.S.C. §§ 15 and 26.

273. Counterclaim-Defendants are engaged in the development, commercialization, and marketing of prescription pharmaceutical products for the treatment of various disorders.

274. Amneal is a supplier of generic pharmaceutical products.

275. Amneal is a potential future direct competitor with Counterclaim-Defendants in the Relevant Market.

276. On information and belief, Counterclaim-Defendants have a predominant share of the Relevant Market.

277. Counterclaim-Defendants have monopoly power in the Relevant Market.

278. Counterclaim-Defendants have exercised monopoly power in the Relevant Market.

EXHIBIT A

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-457

APPROVAL LETTER(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-457

IVAX Research, Inc.
4400 Biscayne Boulevard
Miami, Florida 33137

Attention: Steven M. Viti, Ph.D.
Director, Regulatory Affairs

Dear Dr. Viti:

Please refer to your new drug application (NDA) dated January 30, 2003, received January 31, 2003, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for albuterol sulfate HFA Inhalation Aerosol.

We acknowledge receipt of your submissions dated April 1, May 5 and 15, June 6, 19, and 26, July 15 and 18, August 5, 7, 15, and 29, September 19, October 10, 15, 20 (2) and 30, and November 17, 2003, December 2, 2003, March 15, and 17, April 14, 19, and 29, June 14, and 17, July 20, August 25, September 9, October 6, 8, 11, 18, 19, and 25, 26, 27 (2), 28, 2004.

The April 29, 2004, submission constituted a complete response to our November 28, 2003, action letter.

This new drug application provides for the use of albuterol sulfate HFA Inhalation Aerosol for the treatment or prevention of bronchospasm with reversible obstructive airway disease in adults and children 12 years of age and older.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to, except for including the revisions listed as agreed upon in a telephone conversation with Ms. Akilah Green, on October 29, 2004, the submitted labeling (package insert (copy enclosed), patient leaflet (copy enclosed), and carton and container labeling submitted October 28, 2004).

1. Revise the beginning of the first sentence of the WARNINGS: section of the carton and container labeling submitted October 28, 2004, to "the action of [TRADE NAME] HFA Inhalation Aerosol lasts up to 4 to 6 hours."

2. Revise the last sentence of the first paragraph in parenthesis of the Carcinogenesis, Mutagenesis and Impairment to Fertility section of the Package Insert submitted October 28, 2004, to "(approximately 210 times …)."

3. Remove the graphics from the submitted carton labeling.

These revisions are terms of the NDA approval. Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-457**." Approval of this submission by FDA is not required before the labeling is used.

We have reviewed your proposal requesting that we reconsider your trade name proposal and we object to the tradename (b) (4) as outlined in our letter dated September 29, 2004.

If you choose to use a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit any proprietary name to the Agency for our review prior to its implementation.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring pediatric studies for ages 0 to 11 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of the treatment of bronchospasm with reversible obstructive airway disease in pediatric patients ages 0 to 11.

   Final Report Submission: October 31, 2007

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

We remind you of your agreements listed in your letter dated October 27, 2004, to complete the following:

1. Limit the acceptance criteria for the leachables, (b) (4) (b) (4) and provide Within two months of approval, submit supportive information for these limits and a protocol to conduct a 90-day animal toxicology study to qualify these levels if available information is not sufficient. If after review of the supportive information the Agency decides it is not sufficient and that it will be necessary to conduct the 90-day study in animals, conduct the animal study and submit the final report to the Division within 9 months after FDA feedback on the study is received.

2. Report and consult the Agency for its safety evaluation whenever a previously unspecified leachable has been identified by GC/MS.

3. Submit a validated test method to verify the reliability of the (b) (4) results reported on the manufacturer's COA within 12 months of approval.

4. Submit a correlation study(ies) between levels of leachables in the drug product (through the shelf life or until a plateau is demonstrated) and the extractables from the container closure components of the drug product to the Agency within 12 months of approval.

5. Provide validation data for the GC/MS method used for quantitative determination of leachables in the drug product within 6 months of approval. The drug product specification, (b) (4) will be revised at that time to include the test method for leachables in the drug product, including relative retention times for all identified leachables and all volatile organic compounds (VOC) that are used in the response standard preparation for GC part of the method. In addition, representative chromatograms for response standard preparation will be included at their detection and quantitation limits for a typical sample.

6. Submit a test method and acceptance criteria with supportive data to identify and quantify foreign particulate matter in the drug product to the Agency within 12 months of approval. The acceptance criteria will include limits for particles less than (b) (4) (b) (4) Any non-metallic mineral particulates will be identified and e of asbestos-origin. At that time, the finished product specification (b) (4) will be revised.

7. Provide a Prior Approval Supplement to extend the expiry dating with 24 month stability data from the manually stressed and auto stressed exhibit batches, as well as any stability data of commercial batches available at the time of submission. Data will be submitted electronically in the format previously submitted (i.e., statistical analysis in SAS data transport format).

8. Provide supportive data demonstrating the absence of discernible within-unit APSD trends from beginning to end of inhaler throughout shelf life for the Agency's evaluation prior to modifying the APSD test methodology to test only the beginning of the inhaler for the commercial batches. If needed, the Agency may revisit the appropriateness of the APSD acceptance criteria on the basis of an evaluation of the stability data provided in support of the expiration dating extension.

9. Provide a post-approval submission with supportive data for substituting (b) (4) testing at release on the drug product with (b) (4) results from the COA (b) (4) (b) (4) lots from the (b) (4)

10. Provide a post-approval submission with appropriate data to support reduced (e.g., skip-lot testing) testing schedule for (b) (4) at stability.

11. Provide particle size results and acceptance criteria on COA accompanying each batch of (b) (4) (b) (4) albuterol sulfate that will be received from (b) (4) (b) (4) (b) (4)

If you have any questions, call Akilah Green, Regulatory Project Manager, at (301) 827-5585.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Badrul Chowdhury
10/29/04 05:15:30 PM

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROAIR HFA safely and effectively. See full prescribing information for PROAIR HFA Inhalation Aerosol

PROAIR HFA (albuterol sulfate) INHALATION AEROSOL
Initial U.S. Approval: 1981

----------RECENT MAJOR CHANGES----------
Dosage and Administration 03/12

----------INDICATIONS AND USAGE----------
PROAIR HFA Inhalation Aerosol is a $beta_2$-adrenergic agonist indicated for:
- Treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease. (1.1)
- Prevention of exercise-induced bronchospasm in patients 4 years of age and older. (1.2)

----------DOSAGE AND ADMINISTRATION----------
For oral inhalation only
- Treatment or prevention of bronchospasm in adults and children 4 years of age and older: 2 inhalations every 4 to 6 hours. In some patients, one inhalation every 4 hours may be sufficient. (2.1)
- Prevention of exercise-induced bronchospasm in adults and children 4 years of age and older: 2 inhalations 15 to 30 minutes before exercise. (2.2)
- Priming information: Prime PROAIR HFA before using for the first time, or when the inhaler has not been used for more than 2 weeks. To prime PROAIR HFA, release 3 sprays into the air away from the face. Shake well before each spray. (2.3)
- Cleaning information: At least once a week, wash the actuator with warm water, shake off excess, and air dry thoroughly. (2.3)
- PROAIR HFA inhaler should be discarded when the dose counter displays 0 or after the expiration date on the product, whichever comes first. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
Inhalation Aerosol: Each actuation delivers 108 mcg of albuterol sulfate from the actuator mouthpiece (equivalent to 90 mcg of albuterol base). Supplied in 8.5-g canister containing 200 actuations. (3)

----------CONTRAINDICATIONS----------
Hypersensitivity to albuterol and any other PROAIR HFA Inhalation Aerosol Components. (4)

----------WARNINGS AND PRECAUTIONS----------
- Life-threatening paradoxical bronchospasm may occur. Discontinue PROAIR HFA immediately and treat with alternative therapy. (5.1)
- Need for more doses of PROAIR HFA than usual may be a sign of deterioration of asthma and requires reevaluation of treatment. (5.2)
- PROAIR HFA is not a substitute for corticosteroids. (5.3)
- Cardiovascular effects may occur. Use with caution in patients sensitive to sympathomimetic drugs and patients with cardiovascular or convulsive disorders. (5.4, 5.7)
- Excessive use may be fatal. Do not exceed recommended dose. (5.5)
- Immediate hypersensitivity reactions may occur. Discontinue PROAIR HFA immediately. (5.6)
- Hypokalemia and changes in blood glucose may occur. (5.7, 5.8)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥3.0% and >placebo) are headache, tachycardia, pain, dizziness, pharyngitis, and rhinitis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Teva Respiratory, LLC at 1-888-482-9522 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------DRUG INTERACTIONS----------
- Other short-acting sympathomimetic aerosol bronchodilators and adrenergic drugs: May potentiate effect. (7)
- Beta-blockers: May decrease effectiveness of PROAIR HFA and produce severe bronchospasm. Patients with asthma should not normally be treated with beta-blockers. (7.1)
- Diuretics, or non-potassium sparing diuretics: May potentiate hypokalemia or ECG changes. Consider monitoring potassium levels. (7.2)
- Digoxin: May decrease serum digoxin levels. Consider monitoring digoxin levels. (7.3)
- Monoamine oxidase (MAO) inhibitors and tricyclic antidepressants: May potentiate effect of albuterol on the cardiovascular system. Consider alternative therapy in patients taking MAOs or tricyclic antidepressants. (7.4)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 03/12

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

1 INDICATIONS AND USAGE

1.1 Bronchospasm

PROAIR HFA Inhalation Aerosol is indicated for the treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease.

1.2 Exercise-Induced Bronchospasm

PROAIR HFA Inhalation Aerosol is indicated for the prevention of exercise-induced bronchospasm in patients 4 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Bronchospasm

For treatment of acute episodes of bronchospasm or prevention of symptoms associated with bronchospasm, the usual dosage for adults and children 4 years and older is two inhalations repeated every 4 to 6 hours. More frequent administration or a larger number of inhalations is not recommended. In some patients, one inhalation every 4 hours may be sufficient.

2.2 Exercise-Induced Bronchospasm

The usual dosage for adults and children 4 years of age or older is two inhalations 15 to 30 minutes before exercise.

2.3 Administration Information

Administer PROAIR HFA by oral inhalation only. Shake well before each spray. To maintain proper use of this product and to prevent medication build-up and blockage, it is important to follow the cleaning directions carefully.

Priming: Prime the inhaler before using for the first time and in cases where the inhaler has not been used for more than 2 weeks by releasing three sprays into the air, away from the face.

Cleaning: As with all HFA-containing albuterol inhalers, to maintain proper use of this product and to prevent medication build-up and blockage, it is important to clean the plastic mouthpiece regularly. The inhaler may cease to deliver medication if the plastic actuator mouthpiece is not properly cleaned and dried. To clean: Wash the plastic mouthpiece with warm running water for 30 seconds, shake off excess water, and air dry thoroughly at least once a week**. If the patient has more than one PROAIR HFA inhaler, the patient should wash each one separately to prevent attaching the wrong canister to the wrong plastic actuator. In this way, the patient can be sure to always know the correct number of remaining doses. Never attach a canister of medication from any other inhaler to the PROAIR HFA actuator and never attach the PROAIR HFA canister to an actuator from any other inhaler.** If the mouthpiece becomes blocked, washing the mouthpiece will remove the blockage. If it is necessary to use the inhaler before it is completely dry, shake off excess water, replace canister, spray twice into the air away from face, and take the prescribed dose. After such use, the mouthpiece should be rewashed and allowed to air dry thoroughly. *[see FDA-Approved Patient Labeling (17.9)]*.

Dose Counter: PROAIR HFA has a dose counter attached to the actuator. When the patient receives the inhaler, a black dot will appear in the viewing window until it has been primed 3 times, at which point the number 200 will be displayed. The dose counter will count down each time a spray is released. When the dose counter reaches 20, the color of the numbers will change to red to remind the patient to contact their pharmacist for a refill of medication or consult their physician for a prescription refill. When the dose counter reaches 0, the background will change to solid red. PROAIR HFA inhaler should be discarded when the dose counter displays 0 or after the expiration date on the product, whichever comes first.

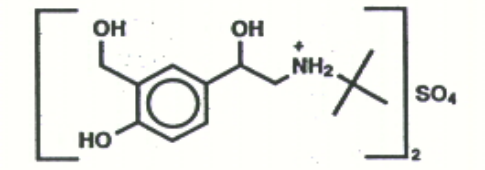
Hypokalemia may also occur. As with all sympathomimetic medications, cardiac arrest and even death may be associated with abuse of PROAIR HFA Inhalation Aerosol.

Treatment consists of discontinuation of PROAIR HFA Inhalation Aerosol together with appropriate symptomatic therapy. The judicious use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. There is insufficient evidence to determine if dialysis is beneficial for overdosage of PROAIR HFA Inhalation Aerosol.

The oral median lethal dose of albuterol sulfate in mice is greater than 2,000 mg/kg (approximately 6,800 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis and approximately 3,200 times the maximum recommended daily inhalation dose for children on a mg/m^2 basis). In mature rats, the subcutaneous median lethal dose of albuterol sulfate is approximately 450 mg/kg (approximately 3,000 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis and approximately 1,400 times the maximum recommended daily inhalation dose for children on a mg/m^2 basis). In young rats, the subcutaneous median lethal dose is approximately 2,000 mg/kg (approximately 14,000 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis and approximately 6,400 times the maximum recommended daily inhalation dose for children on a mg/m^2 basis). The inhalation median lethal dose has not been determined in animals.

11 DESCRIPTION

The active ingredient of PROAIR HFA (albuterol sulfate) Inhalation Aerosol is albuterol sulfate, a racemic salt, of albuterol. Albuterol sulfate has the chemical name α^1-[(*tert*-butylamino) methyl]-4-hydroxy-*m*-xylene-α,α'-diol sulfate (2:1) (salt), and has the following chemical structure:



The molecular weight of albuterol sulfate is 576.7, and the empirical formula is $(C_{13}H_{21}NO_3)_2 \bullet H_2SO_4$. Albuterol sulfate is a white to off-white crystalline powder. It is soluble in water and slightly soluble in ethanol. Albuterol sulfate is the official generic name in the United States, and salbutamol sulfate is the World Health Organization recommended generic name. PROAIR HFA Inhalation Aerosol is a pressurized metered-dose aerosol unit with a dose counter. PROAIR HFA is for oral inhalation only. It contains a microcrystalline suspension of albuterol sulfate in propellant HFA-134a (1, 1, 1, 2-tetrafluoroethane) and ethanol.

Prime the inhaler before using for the first time and in cases where the inhaler has not been used for more than 2 weeks by releasing three sprays into the air, away from the face. After priming, each actuation delivers 108 mcg albuterol sulfate, from the actuator mouthpiece (equivalent to 90 mcg of albuterol base). Each canister provides 200 actuations (inhalations).

This product does not contain chlorofluorocarbons (CFCs) as the propellant.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Albuterol sulfate is a $beta_2$-adrenergic agonist. The pharmacologic effects of albuterol sulfate are attributable to activation of $beta_2$-adrenergic receptors on airway smooth muscle. Activation of $beta_2$-adrenergic receptors leads to the activation of adenylcyclase and to an increase in the intracellular concentration of cyclic-3', 5'-adenosine monophosphate (cyclic AMP). This increase of cyclic AMP is associated with the activation of protein kinase A, which in turn inhibits the phosphorylation of myosin and lowers intracellular ionic calcium

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N021457

Product 001
ALBUTEROL SULFATE (PROAIR HFA) AEROSOL, METERED EQ 0.09MG BASE/INH

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	7105152	09/12/2023		DP			
001	8132712	09/07/2028		DP			03/27/2012
001	9463289	05/18/2031		DP			11/08/2016
001	9808587	05/18/2031		DP			11/16/2017
001	10022509	05/18/2031		DP			08/14/2018
001	10022510	05/18/2031		DP			08/14/2018
001	10086156	05/18/2031		DP			10/17/2018
001	10561808	01/01/2032		DP			03/19/2020
001	10695512	05/18/2031		DP			07/30/2020
001	11395889	05/18/2031		DP			08/19/2022

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
Your search did not return any results		

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION
WASHINGTON, D.C. 20580

Office of the Director
Bureau of Competition

November 7, 2023

By Federal Express

Teva Branded Pharmaceutical
Products R&D, Inc.
Attn: Legal Counsel
c/o Corporate Creations Network Inc.
3411 Silverside Road
Tatnall Building, Ste. 104
Wilmington, New Castle, DE 19810

Re: Improper Orange Book-Listed Patents for QVAR 40, ProAir HFA, ProAir DigiHaler

Dear Teva Counsel:

On September 14, 2023, the Federal Trade Commission ("FTC") issued a Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in the Orange Book.[1] The Policy Statement, a copy of which is appended to this letter, highlights the negative impacts that improper Orange Book patent listings may have on drug competition and notifies market participants "that the FTC intends to scrutinize [such] improper listings as unfair methods of competition in violation of Section 5 of the Federal Trade Commission Act."[2]

This letter is to inform you that we believe certain patents have been improperly or inaccurately listed in the Orange Book with regard to Teva Branded Pharmaceutical Products R&D, Inc's products and that we have availed ourselves of the FDA's regulatory process and submitted patent listing dispute communications to the FDA regarding the patents listed below:[3]

[1] Federal Trade Commission, Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in the Orange Book (Sept. 14, 2023), FTC Policy Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in Orange Book (hereinafter "Policy Statement").
[2] Policy Statement at 1.
[3] The Orange Book listings identified as improper in this chart should not be read as an exhaustive list of every patent that your company may have improperly submitted. Indeed, your firm bears the burden of listing patents in the Orange Book accurately and in accordance with all relevant statutory and regulatory requirements.

NDA	Product Number	Product	Patent Number	Listing Type
21457	1	ProAir HFA	8132712	DP
			9463289	DP
			9808587	DP
			10022509	DP
			10022510	DP
			10086156	DP
			10561808	DP
			10695512	DP
			11395889	DP
205636	2	ProAir DigiHaler	8651103	DP
			8978966	DP
			9216260	DP
			9463288	DP
			9731087	DP
			9782550	DP
			9782551	DP
			10022510	DP
			10124131	DP
			10561808	DP
			10569034	DP
			10765820	DP
			11000653	DP
			11266796	DP
			11351317	DP
			11357935	DP
			11439777	DP
			11464923	DP

20911	2	QVAR 40	9463289	DP
			9808587	DP
			10022509	DP
			10022510	DP
			10086156	DP
			10561808	DP
			10695512	DP
			11395889	DP

As the Policy Statement explains, patents improperly listed in the Orange Book may delay lower-cost generic drug competition. By listing their patents in the Orange Book, brand drug companies may benefit from an automatic, 30-month stay of FDA approval of competing generic drug applications.[4] In addition to delays resulting from such a stay of approval, the costs associated with litigating improperly listed patents may disincentivize investments in developing generic drugs, which risks delaying or thwarting competitive entry. The Supreme Court recognizes that improper Orange Book listings have prevented or delayed generic drug entry since at least the 1990s.[5] Even brief delays in generic competition can reduce patient access to more affordable alternatives and increase costs across the entire health care system.[6]

For decades, the FTC has sought to reduce the anticompetitive effects that result from improperly listing patents in the Orange Book, through enforcement and through amicus briefs articulating that improper listings may violate the antitrust laws.[7] The FTC's Policy Statement serves to reinforce the FTC's concerns about the anticompetitive consequences of improper Orange Book listings and provide notice that the "FTC will continue to use all its tools to halt unlawful business practices that contribute to high drug prices."[8]

As detailed in the Policy Statement, the FTC has several tools at its disposal to address improper Orange Book listings. One of those tools is using the FDA's process to dispute "the accuracy or relevance of patent information submitted" to the FDA for publication in the Orange Book.[9]

[4] Policy Statement at 3 (citing 21 U.S.C. § 355(j)(5)(B)(iii)).
[5] Policy Statement at 3 (citing *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 408 (2012)).
[6] Policy Statement at 4.
[7] Policy Statement at 3; *see also* Decision and Order, *In re Biovail Corp*., FTC Dkt. No. C-4060 (F.T.C. Oct. 2, 2002); Federal Trade Commission's Brief as *Amicus Curiae*, *Jazz Pharms., Inc. v, Avadel CNS Pharms*. No. 1:21-cv-00691 (D. Del. Nov. 10, 2022) (Doc. No. 22-3), https://www.ftc.gov/system/files/ftc_gov/pdf/P163500JazzPharmaAmicusBrief.pdf; *see also* Mem. of Law of *Amicus Curiae* the Federal Trade Commission In Opposition to Defendant's Motion to Dismiss, *In re: Buspirone Patent Litig.*, MDL Docket No. 1410 (S.D.N.Y. Jan. 8, 2002), https://www.ftc.gov/sites/default/files/documents/amicus_briefs/re-buspirone-antitrust-litigation/buspirone.pdf.
[8] Policy Statement at 6.
[9] Policy Statement at 6 (citing 21 C.F.R. § 314.53(f)(1)).

We have opted to use the FDA's regulatory dispute process to address the improper listings, but we retain the right to take any further action the public interest may require, which may include investigating this conduct as an unfair method of competition under Section 5 of the FTC Act, 15 U.S.C. § 45, and as described in the Policy Statement.

Sincerely,

RAHUL RAO Digitally signed by RAHUL RAO Date: 2023.11.07 07:40:38 -05'00'

Rahul Rao
Deputy Director
Bureau of Competition

cc: Brian Savage
General Counsel
Teva Pharmaceuticals USA, Inc.,
400 Interpace Pkwy, Suite 3
Parsippany, NJ 07054
brian.savage@tevapharm.com

Enclosure: FTC Policy Statement Concerning Brand Drug Manufacturers Improper Listing of Patents in the Orange Book

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N020911

Product 002
BECLOMETHASONE DIPROPIONATE (QVAR 40) AEROSOL, METERED 0.04MG/INH
Federal Register determination that product was not discontinued or withdrawn for safety or effectiveness reasons

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
002	9463289	05/18/2031		DP			11/08/2016
002	9808587	05/18/2031		DP			11/30/2017
002	10022509	05/18/2031		DP			08/13/2018
002	10022510	05/18/2031		DP			08/13/2018
002	10086156	05/18/2031		DP			10/16/2018
002	10561808	01/01/2032		DP			03/19/2020
002	10695512	05/18/2031		DP			07/28/2020
002	11395889	05/18/2031		DP			08/19/2022

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
Your search did not return any results		

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N020911

Product 001
BECLOMETHASONE DIPROPIONATE (QVAR 80) AEROSOL, METERED 0.08MG/INH
Federal Register determination that product was not discontinued or withdrawn for safety or effectiveness reasons

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	9463289	05/18/2031		DP			11/08/2016
001	9808587	05/18/2031		DP			11/30/2017
001	10022509	05/18/2031		DP			08/13/2018
001	10022510	05/18/2031		DP			08/13/2018
001	10086156	05/18/2031		DP			10/16/2018
001	10561808	01/01/2032		DP			03/19/2020
001	10695512	05/18/2031		DP			07/28/2020
001	11395889	05/18/2031		DP			08/19/2022

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
Your search did not return any results		

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N207921

Product 002
BECLOMETHASONE DIPROPIONATE (QVAR REDIHALER) AEROSOL, METERED 0.08MG/INH

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
002	8132712	09/07/2028		DP			08/28/2017
002	8931476	07/17/2031		DP			08/28/2017
002	10022509	05/18/2031		DP			08/13/2018
002	10022510	05/18/2031		DP			08/13/2018
002	10086156	05/18/2031		DP			10/16/2018
002	10561808	01/01/2032		DP			03/19/2020
002	10695512	05/18/2031		DP			07/28/2020
002	10792447	01/25/2039		DP			10/29/2020
002	11395888	01/26/2038		DP			08/19/2022
002	11395889	05/18/2031		DP			08/19/2022
002	11559637	07/21/2039		DP			02/22/2023

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
002	11583643	08/19/2041		DP			03/20/2023

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
Your search did not return any results		

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N205636

Product 002
ALBUTEROL SULFATE (PROAIR DIGIHALER) POWDER, METERED EQ 0.09MG BASE/INH

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
002	7540282	05/06/2023		DP			01/09/2019
002	8651103	03/26/2028		DP			01/09/2019
002	8978966	01/13/2032		DP			01/09/2019
002	9216260	06/28/2031		DP			01/09/2019
002	9463288	05/19/2025		DP			01/09/2019
002	9731087	05/18/2031		DP			01/09/2019
002	9782550	08/28/2035		DP			01/09/2019
002	9782551	08/28/2035		DP			01/09/2019
002	10022510	05/18/2031		DP			01/09/2019
002	10124131	05/18/2031		DP			01/09/2019
002	10561808	01/01/2032		DP			03/19/2020

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
002	10569034	08/16/2036		DP			03/12/2020
002	10765820	05/19/2025		DP			10/06/2020
002	10918816	12/14/2035		DP			03/18/2021
002	11000653	12/18/2038		DP			06/10/2021
002	11173259	07/06/2040		DP			12/08/2021
002	11266796	02/22/2041		DP			04/07/2022
002	11344685	09/26/2039		DP			06/29/2022
002	11351317	02/10/2038		DP			06/29/2022
002	11357935	09/24/2038		DP			07/13/2022
002	11439777	05/24/2040		DP			10/06/2022
002	11464923	06/19/2040		DP			11/10/2022

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
Your search did not return any results		

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N205636

Product 001
ALBUTEROL SULFATE (PROAIR RESPICLICK) POWDER, METERED EQ 0.09MG BASE/INH

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	7540282	05/06/2023		DP			04/28/2015
001	8651103	03/26/2028		DP			04/28/2015
001	8978966	01/13/2032		DP			01/21/2016
001	9216260	06/28/2031		DP			01/21/2016
001	9463288	05/19/2025		DP			11/08/2016
001	9731087	05/18/2031		DP			08/31/2017
001	10022510	05/18/2031		DP			08/14/2018
001	10124131	05/18/2031		DP			12/12/2018
001	10561808	01/01/2032		DP			03/19/2020
001	10765820	05/19/2025		DP			10/06/2020

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
Your search did not return any results		

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N208798

Product 001
FLUTICASONE PROPIONATE (ARMONAIR RESPICLICK) POWDER 0.055MG/INH

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	7540282	05/06/2023		DP			01/30/2017
001	7540282*PED	11/06/2023					
001	8651103	03/26/2028		DP			01/30/2017
001	8651103*PED	09/26/2028					
001	8714149	02/25/2032		DP			01/30/2017
001	8714149*PED	08/25/2032					
001	8978966	01/13/2032		DP			01/30/2017
001	8978966*PED	07/13/2032					
001	9216260	06/28/2031		DP			01/30/2017
001	9216260*PED	12/28/2031					
001	9463288	05/19/2025		DP			01/30/2017
001	9463288*PED	11/19/2025					

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	9616024	09/01/2024		DP			05/10/2017
001	9616024*PED	03/01/2025					
001	9731087	05/18/2031		DP			08/31/2017
001	9731087*PED	11/18/2031					
001	10022510	05/18/2031		DP			08/13/2018
001	10022510*PED	11/18/2031					
001	10124131	05/18/2031		DP			12/12/2018
001	10124131*PED	11/18/2031					
001	10195375	02/14/2031		DP			03/05/2019
001	10195375*PED	08/14/2031					
001	10561808	01/01/2032		DP			03/19/2020
001	10561808*PED	07/01/2032					
001	10765820	05/19/2025		DP			10/06/2020
001	10765820*PED	11/19/2025					

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
001	**NPP**	07/09/2024
001	**NPP** ***PED**	01/09/2025

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N208798

Product 004
FLUTICASONE PROPIONATE (ARMONAIR DIGIHALER) POWDER 0.055MG/INH

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
004	7540282	05/06/2023		DP			03/20/2020
004	7540282*PED	11/06/2023					
004	8651103	03/26/2028		DP			03/20/2020
004	8651103*PED	09/26/2028					
004	8714149	02/25/2032		DP			03/20/2020
004	8714149*PED	08/25/2032					
004	8978966	01/13/2032		DP			03/20/2020
004	8978966*PED	07/13/2032					
004	9216260	06/28/2031		DP			03/20/2020
004	9216260*PED	12/28/2031					
004	9463288	05/19/2025		DP			03/20/2020
004	9463288*PED	11/19/2025					

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
004	9616024	09/01/2024		DP			03/20/2020
004	9616024*PED	03/01/2025					
004	9731087	05/18/2031		DP			03/20/2020
004	9731087*PED	11/18/2031					
004	9782550	08/28/2035		DP			03/20/2020
004	9782550*PED	02/28/2036					
004	9782551	08/28/2035		DP			03/20/2020
004	9782551*PED	02/28/2036					
004	10022510	05/18/2031		DP			03/20/2020
004	10022510*PED	11/18/2031					
004	10124131	05/18/2031		DP			03/20/2020
004	10124131*PED	11/18/2031					
004	10195375	02/14/2031		DP			03/20/2020
004	10195375*PED	08/14/2031					
004	10561808	01/01/2032		DP			03/19/2020
004	10561808*PED	07/01/2032					
004	10569034	08/16/2036		DP			03/12/2020
004	10569034*PED	02/16/2037					
004	10765820	05/19/2025		DP			10/06/2020
004	10765820*PED	11/19/2025					
004	10918816	12/14/2035		DP			03/18/2021
004	10918816*PED	06/14/2036					
004	11000653	12/18/2038		DP			06/10/2021
004	11000653*PED	06/18/2039					
004	11173259	07/06/2040		DP			12/08/2021
004	11173259*PED	01/06/2041					
004	11266796	02/22/2041		DP			04/07/2022
004	11266796*PED	08/22/2041					
004	11344685	09/26/2039		DP			06/29/2022
004	11344685*PED	03/26/2040					
004	11351317	02/10/2038		DP			06/29/2022
004	11351317*PED	08/10/2038					
004	11357935	09/24/2038		DP			07/13/2022
004	11357935*PED	03/24/2039					
004	11439777	05/24/2040		DP			10/06/2022

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
004	11439777*PED	11/24/2040					
004	11464923	06/19/2040		DP			11/10/2022
004	11464923*PED	12/19/2040					

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
004	NPP	07/09/2024
004	NPP *PED	01/09/2025

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N208799

Product 004
FLUTICASONE PROPIONATE; SALMETEROL XINAFOATE (AIRDUO DIGIHALER)
POWDER 0.055MG/INH;EQ 0.014MG BASE/INH

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
004	7540282	05/06/2023		DP			08/02/2019
004	7540282*PED	11/06/2023					
004	8651103	03/26/2028		DP			08/02/2019
004	8651103*PED	09/26/2028					
004	8714149	02/25/2032		DP			08/02/2019
004	8714149*PED	08/25/2032					
004	8978966	01/13/2032		DP			08/02/2019
004	8978966*PED	07/13/2032					
004	9066957	10/06/2034		DP	**U-645**		08/02/2019
004	9066957*PED	04/06/2035					
004	9216260	06/28/2031		DP			08/02/2019

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
004	9216260*PED	12/28/2031					
004	9415008	10/06/2034		DP	U-645		08/02/2019
004	9415008*PED	04/06/2035					
004	9463288	05/19/2025		DP			08/02/2019
004	9463288*PED	11/19/2025					
004	9616024	09/01/2024		DP			08/02/2019
004	9616024*PED	03/01/2025					
004	9731087	05/18/2031		DP			08/02/2019
004	9731087*PED	11/18/2031					
004	9782550	08/28/2035		DP			08/02/2019
004	9782550*PED	02/28/2036					
004	9782551	08/28/2035		DP			08/02/2019
004	9782551*PED	02/28/2036					
004	9987229	09/01/2024		DP			08/02/2019
004	9987229*PED	03/01/2025					
004	10022510	05/18/2031		DP			08/02/2019
004	10022510*PED	11/18/2031					
004	10124131	05/18/2031		DP			08/02/2019
004	10124131*PED	11/18/2031					
004	10195375	02/14/2031		DP			08/02/2019
004	10195375*PED	08/14/2031					
004	10561808	01/01/2032		DP			03/19/2020
004	10561808*PED	07/01/2032					
004	10569034	08/16/2036		DP			03/12/2020
004	10569034*PED	02/16/2037					
004	10765820	05/19/2025		DP			10/06/2020
004	10765820*PED	11/19/2025					
004	10918816	12/14/2035		DP			03/18/2021
004	10918816*PED	06/14/2036					
004	11000653	12/18/2038		DP			06/10/2021
004	11000653*PED	06/18/2039					
004	11173259	07/06/2040		DP			12/08/2021
004	11173259*PED	01/06/2041					
004	11266796	02/22/2041		DP			04/07/2022
004	11266796*PED	08/22/2041					

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
004	11344685	09/26/2039		DP			06/29/2022
004	11344685*PED	03/26/2040					
004	11351317	02/10/2038		DP			06/29/2022
004	11351317*PED	08/10/2038					
004	11357935	09/24/2038		DP			07/13/2022
004	11439777	05/24/2040		DP			10/06/2022
004	11464923	06/19/2040		DP			11/10/2022

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
004	**M-61**	07/09/2024
004	**M-61** ***PED**	01/09/2025

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

/ **Orange Book Home (index.cfm)**

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Home (index.cfm?resetfields=1) | **Back to Product Details**

Additional Information about Patents

- Patent information is published on or after the submission date as defined in 21 CFR 314.53(d)(5).
- Patent listings published prior to August 18, 2003, only identify method-of-use claims. The listed patents may include drug substance and/or drug product claims that are not indicated in the listing.
- As of December 5, 2016, an NDA holder submitting information on a patent that claims both the drug substance and the drug product (and is eligible for listing on either basis) is required only to specify that it claims either the drug substance or the drug product. Orange Book users should not rely on an Orange Book patent listing, regardless of when first published, to determine the range of patent claims that may be asserted by an NDA holder or patent owner.

Patent and Exclusivity for: N208799

Product 001
FLUTICASONE PROPIONATE; SALMETEROL XINAFOATE (AIRDUO RESPICLICK)
POWDER 0.055MG/INH;EQ 0.014MG BASE/INH

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	7540282	05/06/2023		DP			01/30/2017
001	7540282*PED	11/06/2023					
001	8651103	03/26/2028		DP			01/30/2017
001	8651103*PED	09/26/2028					
001	8714149	02/25/2032		DP			01/30/2017
001	8714149*PED	08/25/2032					
001	8978966	01/13/2032		DP			01/30/2017
001	8978966*PED	07/13/2032					
001	9066957	10/06/2034		DP	**U-645**		01/30/2017
001	9066957*PED	04/06/2035					
001	9216260	06/28/2031		DP			01/30/2017

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	9216260*PED	12/28/2031					
001	9415008	10/06/2034		DP	U-645		01/30/2017
001	9415008*PED	04/06/2035					
001	9463288	05/19/2025		DP			01/30/2017
001	9463288*PED	11/19/2025					
001	9616024	09/01/2024		DP			05/10/2017
001	9616024*PED	03/01/2025					
001	9731087	05/18/2031		DP			08/31/2017
001	9731087*PED	11/18/2031					
001	9987229	09/01/2024		DP			07/03/2018
001	9987229*PED	03/01/2025					
001	10022510	05/18/2031		DP			08/13/2018
001	10022510*PED	11/18/2031					
001	10124131	05/18/2031		DP			12/12/2018
001	10124131*PED	11/18/2031					
001	10195375	02/14/2031		DP			03/05/2019
001	10195375*PED	08/14/2031					
001	10561808	01/01/2032		DP			03/19/2020
001	10561808*PED	07/01/2032					
001	10765820	05/19/2025		DP			10/06/2020
001	10765820*PED	11/19/2025					

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration
001	M-61	07/09/2024
001	M-61 *PED	01/09/2025

View a list of all patent use codes (results_patent.cfm)
View a list of all exclusivity codes (results_exclusivity.cfm)

Confidential Material Excerpted Under Protective Order

Appx916-917

Confidential Material Excerpted Under Protective Order

Appx921-952

APPENDIX C

UNIFORM TERMS

DOSAGE FORMS

AEROSOL, FOAM
AEROSOL, METERED
CAPSULE
CAPSULE, DELAYED REL PELLETS
CAPSULE, DELAYED RELEASE
CAPSULE, EXTENDED RELEASE
CAPSULE, PELLETS
CAPSULE, TABLET
CAPSULE, TABLET, TABLET
CLOTH
CONCENTRATE
CREAM
CREAM, AUGMENTED
CREAM, INSERT
ELIXIR
EMULSION
ENEMA
FILM
FILM, EXTENDED RELEASE
FOAM
FOR SOLUTION
FOR SUSPENSION
FOR SUSPENSION, DELAYED RELEASE
FOR SUSPENSION, EXTENDED RELEASE
GAS
GEL
GEL, AUGMENTED
GEL, METERED
GRANULE
GRANULE, DELAYED RELEASE
GRANULES
GRANULES, EXTENDED RELEASE
GUM, CHEWING
IMPLANT
INHALANT
INJECTABLE
INJECTABLE, LIPID COMPLEX
INJECTABLE, LIPOSOMAL
INJECTION, EXTENDED RELEASE
INSERT
INSERT, EXTENDED RELEASE
INTRAUTERINE DEVICE
JELLY
LIQUID
LOTION
LOTION, AUGMENTED
LOTION/SHAMPOO
OIL
OIL/DROPS
OINTMENT
OINTMENT, AUGMENTED
PASTE
PATCH
PELLET
PELLETS
POWDER
POWDER, EXTENDED RELEASE
POWDER, METERED
RING
SHAMPOO
SOLUTION
SOLUTION FOR SLUSH
SOLUTION, EXTENDED RELEASE
SOLUTION, GEL FORMING/DROPS
SOLUTION, METERED
SOLUTION/DROPS
SPONGE
SPRAY
SPRAY, METERED
SUPPOSITORY
SUSPENSION
SUSPENSION, EXTENDED RELEASE
SUSPENSION, LIPOSOMAL
SUSPENSION/DROPS
SWAB
SYRUP
SYSTEM
TABLET
TABLET, CHEWABLE
TABLET, DELAYED RELEASE
TABLET, EFFERVESCENT
TABLET, EXTENDED RELEASE
TABLET, EXTENDED RELEASE, CHEWABLE
TABLET, FOR SUSPENSION
TABLET, ORALLY DISINTEGRATING
TABLET, ORALLY DISINTEGRATING, DELAYED RELEASE
TABLET, ORALLY DISINTEGRATING, EXTENDED RELEASE
TAPE
TROCHE/LOZENGE

Note: Terms comprise currently marketed products

Tertiary patenting on drug–device combination products in the United States

Reed F Beall & Aaron S Kesselheim

Drug–device combination products are becoming increasingly prevalent, with many lasting years beyond the expiration date of primary and secondary patents on the drug itself.

The epinephrine autoinjector (EpiPen) treatment for anaphylaxis has been making headlines since 2016 for price increases of over 400%, even though epinephrine was isolated over 100 years ago[1–4]. Investigations by the United States Congress have revealed the primary reason for such price increases: there are four patents on epinephrine's special delivery device that do not expire until 2024 (ref. 5). These patents have made it impossible for other manufacturers to copy the EpiPen delivery system, preventing low-cost generic competition. Patents only last 20 years, but 2024 would mark 37 years since the EpiPen was approved for marketing in the United States in 1987.

Other drug–device combinations like the EpiPen are protected by patents on the drug delivery devices. One survey of patent data on a sample of 49 combination products for asthma, chronic obstructive pulmonary disease, diabetes, and anaphylaxis found that over half of the current patents were directed to the device itself[6]. Such patents allow manufacturers to raise prices by blocking generic competition in those markets[7–10]. One study of insulin pens found that the number of patents listed with the US Food and Drug Administration (FDA) on these combination products more than doubled between 2004 and 2014, coincident with an increase in prices on the products[11].

It is unknown how common drug delivery device patents are across all drug classes. To assist policymakers in understanding the causes for, and solutions to, high drug prices, and in updating and modernizing approaches to regulation of combination products[12], we sought to evaluate the prevalence of drug delivery device patents in the United States and the extent to which they block potential low-cost generic competition (**Box 1**). Since drug delivery devices can be updated and repatented incrementally (e.g., different components on an injector pen), we expected to find more drug delivery device patents to accrue over time, and consequently, to expire later than other kinds of patents.

Reed F. Beall & Aaron S. Kesselheim are at the Program On Regulation, Therapeutics, And Law (PORTAL), Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA.
e-mail: akesselheim@bwh.harvard.edu

RESULTS

In the four years covered in our study, we found 1,784 distinct drug products associated with one or more patents, and 5,056 patents in total. About 7% (369) of these were tertiary patents and were associated with 144 drug–device combination products. The most common such products were inhalers (31%, 45/144), injector pens (24%, 34/144), and patches (18%, 26/144). These 144 products could be traced to 66 different manufacturers, with most coming from GlaxoSmithKline (9%, 13/144), AstraZeneca (6%, 9/144), Eli Lilly (6%, 9/144), Novo Nordisk (6%, 9/144), and Novartis (6%, 8/144). **Supplementary Table 1** includes our full product sample and the relevant descriptive characteristics of these products and patents.

Changes in prevalence of primary, secondary, and tertiary patents over time. The proportion of patents classified as tertiary patents tripled from 3% (27/916) in the year 2000 to 9% (295/3,464) in 2016. Among all drug products associated with one or more patents, the proportion with a device patent increased from 3% (18/614) in the year 2000 to 10% (109/1,135) in 2016 (**Table 1**).

In 2000, there were 42 drug–device combination products (among 614 total drugs) and 85 associated patents. These 85 patents included 3 (4%) primary patents, 53 (62%) secondary patents, and 29 (34%) tertiary patents. A median of two patents (interquartile range, IQR: 0 to 4) were cited per drug–device combination product.

In 2005, there were 68 drug–device combination products (among 835 total drugs) and 179 associated patents. These 179 patents included 9 (5%) primary patents, 109 (69%) secondary patents, and 61 (34%) tertiary patents. A median of two patents (IQR: 1 to 4) were cited per drug–device combination product.

In 2010, there were 95 drug–device combination products (among 997 total drugs) and 416 associated patents. These 416 patents included 29 (7%) primary patents, 197 (47%) secondary patents, and 190 (46%) tertiary patents. A median of three patents (IQR: 2 to 6) were cited per drug–device combination product.

In 2016, there were 127 drug–device combination products (among 1,135 total drugs) and 844 associated patents. These 844 patents included 64 (8%) primary patents, 302 (36%) secondary patents, and 478 (57%) tertiary patents. A median of four patents (IQR: 2 to 11) were cited per drug–device combination product.

Reasons for changes in tertiary patent prevalence. We observed three major factors contributing to the increasing prevalence of tertiary patents. First, tertiary patents played a growing role in combination products' patent portfolios (**Fig. 1**). This change was driven in part by a growing number of products listing only tertiary patents and no other patents covering the drug. Overall, 22% (32/144) of the products listed only tertiary patents during any of the years in which they were being actively marketed. The number products only citing tertiary patents climbed from 21% (9/42) in

Table 1 Proportion of tertiary patents relative to all patents and all patented products

Year	All patents	Tertiary patents, *N* (%)	All drug products listing one or more patents[a]	Drug products listing a drug delivery device patent, *N* (%)[a]
2000	916	27 (3)	614	18 (3)
2005	1,593	61 (4)	835	35 (4)
2010	2,069	135 (7)	997	59 (6)
2016	3,464	295 (9)	1,135	109 (10)

[a]Products were counted by new drug application (NDA) numbers.

2000 to 22% (15/68) in 2005 to 22% (21/95) in 2010, and to 25% (32/128) in 2016.

Second, a growing subset of products listed high numbers of tertiary patents. In 2000, only 4 drug–device combination products (out of 42, 10%) cited 3 such patents. By 2016, 53 (out of 127, 41%) listed 3 or more, and 17 (13%) listed 10 or more. For example, the autoinjector Evzio (naloxone) for treating opioid overdoses and Auvi-Q (epinephrine) each cited more than 20 tertiary patents in 2016.

Third, the same products accrued more drug delivery device patents over time. Of the 144 products in our main sample, 94 (65%) were marketed during two or more of the four time points we studied. Of those 94 products, 47 (50%) did not have a tertiary patent listed in the first year it appeared in our database but did have one listed in a later year. Over half (59%, 55/94) had more tertiary patents listed in a later year than in an earlier one. For example, Sumavel DosePro (sumatriptan injection) for migraine headaches had three tertiary patents in 2010, but nine by 2016. In other cases, modified formulations were introduced as new product lines with novel trade names, bearing more tertiary patents. For example, AstraZeneca's Pulmicort Respules (budesonide inhalation suspension) had one tertiary patent in 2005 and none in 2010, while its newer Pulmicort Flexhaler (budesonide inhalation powder) appeared in 2010 with two tertiary patents.

Last-expiring patents on drug–device combination products. Tertiary patents were the last to expire in 70% (101/144) of the sample, expiring a median of 4.7 years (IQR: –0.5 to 11.6) after all others. Among the 144 products were 31 that exclusively listed tertiary patents. These products had been on the market for a median of 15.2 years (IQR: 6.1 to 20.7). These products' last-expiring tertiary patents ended a median of 16.5 years (IQR: 12.7 to 19.7) after FDA approval.

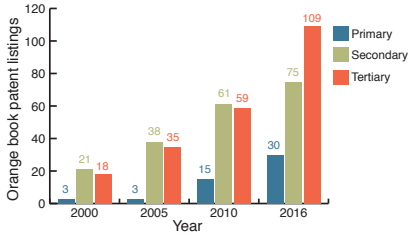


Figure 1 Changes in prevalence of primary, secondary, and tertiary patents over time. By 2016, the number of tertiary patents for drug–device combination products in the Orange Book had overtaken those of other patent types.

Among the 144 products in the main sample, 113 had tertiary device and other non-device (primary or secondary) patents available for comparison of their expiration dates. These 112 products were relatively newer and were approved a median of 11.2 years ago (IQR: 4.9 to 16.9). These products' last-expiring tertiary patent was a median of 16.5 years (IQR: 13.0 to 21.6) after FDA approval as compared to a median of 15.2 years (IQR: 12.3 to 18.3) for all other patent types. This difference was most pronounced among the 22 injector pens with a median difference of 6.6 years (IQR: 3.8 to 10.1) as compared to a median difference of 1.4 years (IQR: –1.8 to 5.2) among the 42 inhalers and of 0.0 years (IQR: –1.7 to 4.2) among the 20 patches.

Among these 113 drugs, 32 had all three patent types available for comparison of their expiration dates. There was a median of 12.4 years (IQR: 9.9 to 15.0) between those products' FDA approvals and the expiration of the last-expiring primary patent, a median of 0.2 additional years (IQR: 0.0 to 4.8) to the expiration of the last secondary patent, and a median of 4.4 additional years (IQR: –1.8 to 7.3) to the expiration of the last tertiary patent.

Three overlapping layers of patent protection on drug–device combinations. **Figure 2** shows the differences in patent counts and their expiration dates relative to FDA approval for all patents by type for the 42 drug–device combination products in 2000 as compared to the 127 drug–device combination products in 2016. For these products, by 2016, tertiary patents outnumbered and outlasted secondary patents (which in turn outnumbered and outlasted primary patents); by contrast, in 2000, secondary patents were more prevalent.

DISCUSSION

Patents listed with the FDA related to drug delivery devices have more than tripled since 2000. These tertiary patents, as we have labeled them, contributed a median of 4.7 years of additional patent protection for drug–device combination products beyond the primary and secondary patents, with such market exclusivity extensions being particularly common among pens and inhalers. In 2016, 32 drug products were covered exclusively by tertiary patents.

Our finding that tertiary patents are being listed in the Orange Book[5] and that they typically expire later than other patent types implies that for these products, generic versions are prevented from entering the market for longer than would otherwise be the case. If manufacturers could not list drug delivery device patents in the Orange Book, the median product in our sample would have had 13.9 years (IQR: 3.2 to 17.1) of patent life remaining after FDA approval, as compared to the current situation in which the median is 17.3 years (IQR: 14.8 to 22.2). Aside from the difference of 3.4 years between these scenarios, the removal of device patents from the Orange Book would immediately clear the FDA to review applications from generic companies for 38 drugs in 2016. These factors increase the risk that such drugs will be subject to price increases.

Generic manufacturers seeking FDA approval before the expiration of tertiary patents must make a special certification (known as a "Paragraph IV certification") that the reference product's patents are either irrelevant or invalid (**Supplementary Table 2**). Other studies have found that such patent challenges are undertaken less frequently for products in smaller, more specialized markets and consequently lead to longer market exclusivity periods[13]. We note that only 22% (32/144) of the drugs in our sample appeared on the FDA's list of drugs with a patent challenge, while a generic therapeutic equivalent was listed in the Orange Book for only 12. By contrast, such patent challenges are the norm for blockbuster drugs. Thus, drug–device combination products covered by tertiary patents may face fewer patent challenges and even weak tertiary patents may go unchallenged in these markets and successfully delay FDA approval for many years.

Another implication of our study is that manufacturers appear to be continuously modifying and repatenting the designs of drug delivery devices for combination drug–device products. While some of these changes may have therapeutic value, they also may increase the risk of product recalls, manufacturing errors, and device failures, as well as require re-education of physicians and patients in how to use the updated device. For example, GlaxoSmithKline's Ventolin HFA (albuterol sulfate) inhaler was recently recalled for a leaky

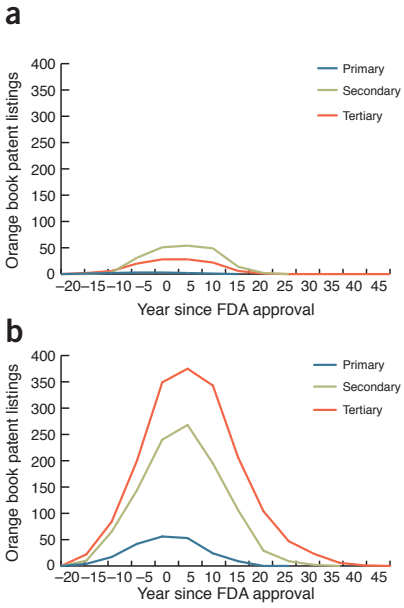


Figure 2 Duration of unexpired primary, secondary, and tertiary patents for drug–device combination products in 2000 and 2016 (relative to FDA approval date). (**a**) Breakdown of Orange Book patents for 42 drug–device combination products in 2000. (**b**) Breakdown of Orange Book patents for 127 drug–device combination products in 2016.

canister, a component of the device covered by many Orange Book–listed patents[14]. Similarly, GlaxoSmithKline's Advair Diskus (fluticasone propionate and salmeterol inhalation powder) was recently recalled owing to problems relating to the device delivering fewer doses than was indicated on the dose counter, a patented subcomponent of the device[15]. Other products captured in our study with recalls flagged by the FDA as having "defective delivery systems" also include Tudorza Pressair (aclidinium bromide inhalation powder), Qnasl (beclomethasone dipropionate), Combivent Respimat (ipratropium bromide and albuterol), Auvi-Q, and the Epipen[16,17].

A number of policy options could be appropriate for this area. One possible approach would be to confine sponsors to listing patents in the Orange Book only at the time of filing their initial application with the FDA. This would restrict companies from adding patents on a rolling basis to the Orange Book without simultaneously providing clinical trials to support product changes. Another option is to make Orange Book patent listing more selective by making only primary patents listable or barring the listing of device patents entirely. Other countries have established patent review bodies within their drug regulators to ensure that newly listed patents cover product changes that confer additional clinical benefit, which is not among the legal criteria for obtaining the patent in the first place[18].

Our study was limited in that our methodology relies upon tertiary patent listings to identify combination products. Consequently, we may not have captured combination products without patents or those that have only listed non-device patents. The FDA does not currently maintain a list of drug–device combination products nor does it have a field within its current databases that indicate such combinations[19]. However, a previous study searched by products' active ingredients, rather than using device patents to locate combination products, and we found that it was nearly universal for combination products to include at least one device patent[6].

Other factors not observed by this study may also contribute toward the apparent proliferation of tertiary patents or lack of generic competition in drug–device combination markets, such as those related to the specialized nature of these markets and challenges in determining interchangeability between two different devices delivering the same drug. The absence of generic insulin in the United States, for example, is clearly affected by fac-

Box 1 Methods

Brand-name drug manufacturers are required by law to list in the FDA's *Approved Drug Products with Therapeutic Equivalence* register (the "Orange Book") patents that they consider essential in protecting their prescription drug products. We obtained electronic copies of the Orange Book's[5] 'patent' and 'product' tables from the FDA for the years 2000, 2005, 2010, and 2016. These provide four snapshots in time of the small-molecule drug market with respect to the products available (brand-name and generic) and with respect to the patents protecting brand-name products. Because the FDA considers drug delivery devices to be inseparable from the medicines that they contain, manufacturers are permitted to list in the Orange Book patents covering such devices along with patents on the drug active ingredient and other patents on the drug itself, such as the crystal structure, salt, and methods of use[10]. We linked patent numbers listed in the Orange Book for each of the four years to LexisNexis TotalPatent, an international patent database, and extracted patent titles, abstracts, and claims (http://www.lexisnexis.com/totalpatent/signonForm.do).

For each patent, we used a two-step screening procedure to code them as covering drug delivery devices or the drug itself. The first step was to screen for device patents by reviewing each patent's title and abstract, which was followed by full text review when necessary to confirm device designations. Drug delivery device patents were those that described a device, implement or encasing (or a part thereof) used to deliver, preserve, distribute, dispense, or properly apply or ingest the medicament in the correct dosage and/or at the correct time.

Among non-device patents, we extracted the data from the electronic Orange Book 'substance patent' field, which indicates whether the manufacturer considers the patent in question to be integral to the drug's active ingredient. We coded these active-ingredient-related patents as 'primary patents'. The remaining patents therefore pertained to more peripheral aspects of the drug, including its formulation (e.g., extended release) or its indications. We coded these as 'secondary patents'. Since drug delivery device patents are even more peripheral than secondary patents on the drug itself, we designated these as 'tertiary patents'.

From the Orange Book, we imported into our database essential information about the products, including the trade names, active ingredients, strengths, dosage forms, routes of administration, manufacturers, marketing status (discontinued vs. actively marketed), and approval dates. We included all products with a tertiary patent cited at any time point in our study in which the product was being actively marketed (i.e., it had not been discontinued). In doing so, our data still captured products' patent portfolios before and after the expiration of any tertiary patent listings (i.e., some products had tertiary patent listings for some time points in our study, but not others).

Our analysis included a tabulation of the counts of each of the three patent types (primary, secondary, tertiary) by product and collectively across the sample for each year in our study. We also assessed the number of years between FDA approval and the last-expiring patent of each type by product and collectively for each time point. Another variable considered was the current age of products (i.e., the years between FDA approval and January 1, 2017).

tors other than the tertiary patents or even patents on the insulins themselves[20]. Still, we found that these manufacturers continue to redevelop and repatent their pen delivery devices. As another example, the FDA mandatory switch away from ozone-depleting emissions from inhalers—a process which has been negotiated and introduced progressively since 1997 (ref. 21)—may have contributed to some extent to manufacturers' device design updates. Nonetheless, companies have continued to update these devices well after that time.

Finally, some patents (regardless of type) were cited by multiple products. To reduce double-counting, we have reported statistics on the unique number of patents as well as the number of product–patent combinations listed.

Conclusions

The practice of listing tertiary patents for combination products in the Orange Book is accelerating. As tertiary patents may be added progressively over time, they may extend patent life well beyond the life of all other patents and substantially delay competitors from gaining FDA approval, which makes these markets especially vulnerable to high prices. Should reform be considered, options include limiting the types of listable patents in the Orange Book. Similarly, any product that is different enough from the reference product to earn a new patent could require more explicit clinical evidence to demonstrate its safety and efficacy. These measures would discourage excessive redevelopment and repatenting of drug–device combination products, and open markets to lower-cost generics sooner.

Note: Any Supplementary Information and Source Data files are available in the online version of the paper.

ACKNOWLEDGMENTS

A.S.K.'s work is supported by the Laura and John Arnold Foundation and Harvard Program in Therapeutic Science, with additional support from the Engelberg Foundation. The authors are grateful to J.W. Nickerson, W.A. Kaplan, and A. Attaran for their feedback on developing this idea, as well as to J.J. Darrow and M.S. Sinha for their insights on earlier drafts.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

1. Rubin, R. *Lancet* **388**, 1266 (2016).
2. Duhigg, C. Outcry over EpiPen prices hasn't made them lower. *The New York Times* (4 June 2017).
3. Kasperkevic, J. New York investigates EpiPen maker Mylan after price hike of medication. *The Guardian* (6 September 2016).
4. Cha, A.E. US lawmakers demand investigation of $100 price hike of lifesaving EpiPens. *The Washington Post* (23 August 2016).
5. US Food and Drug Administration. *Approved Drug Products with Therapeutic Equivalence Evaluations 2017* (FDA, 2017).
6. Beall, R.F., Nickerson, J.W., Kaplan, W.A. & Attaran, A. *PLoS One* **11**, e0148939 (2016).
7. AstraZeneca. Health Canada endorsed important safety information on Pulmicort Turbuhaler (budesonide) powder for oral inhalation, 200 µg per metered dose (23 July 2012). http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2012/15087a-eng.php
8. Rosenthal, E. The soaring cost of a simple breath. *The New York Times* (12 October 2013).
9. Rosenthal, E. Even small medical advances can mean big jumps in bills. *The New York Times* (5 April 2014).
10. Mahn, T.G. *et al. Pharm. Law Industry Report* **9** PLIR 1500 (2 December 2011).
11. Luo, J. & Kesselheim, A.S. *Lancet Diabetes Endocrinol.* **3**, 835–837 (2015).
12. Hunter, N.L. & Sherman, R.E. *Nat. Rev. Drug Discov.* **16**, 513–514 (2017).
13. Grabowski, H.G. & Kyle, M. *Manage. Decis. Econ.* **28**, 491–502 (2007).
14. The GoodRx Pharmacist. FDA recalls Ventolin HFA for asthma. *GoodRx* https://www.goodrx.com/blog/fda-recalls-ventolin-hfa-for-asthma/ (14 April 2017).
15. Herbert, G. Asthma inhaler recall: GSK says nearly 600,000 may have defect. *The Post-Standard* (6 April 2017).
16. Palmer, E. AstraZeneca again recalling inhalers. *FiercePharma* (24 March 2016).
17. US Food and Drug Administration. *Enforcement Report* https://www.accessdata.fda.gov/scripts/ires/index.cfm (FDA, 2017).
18. Government of Canada. Guidance Document: Patented Medicines (Notice of Compliance) Regulations (27 October, 2016). https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/patented-medicines/notice-compliance-regulations.html
19. US Food and Drug Administration. *Combination Products* https://www.fda.gov/combinationproducts/default.htm (FDA, 2017).
20. Greene, J.A. & Riggs, K.R. *N. Engl. J. Med.* **372**, 1171–1175 (2015).
21. US Food and Drug Administration. Phase-out of CFC metered-dose inhalers https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm063054.htm (2013).

II. SCOPE

The Center for Devices and Radiological Health has been asked questions on a number of important issues related to the preparation of a 510(k) premarket notification for nebulizers, metered dose inhalers, and other related components such as actuators and spacers. This document is intended to respond to many of these questions and to provide a general awareness of the present perspectives held by the FDA on issues related to these devices. FDA regards all nebulizers and MDI's as prescription devices. The device manufacturer must have a cleared 510(k) premarket notification before marketing the device.

This reviewer guidance document suggests the importance of environmental testing, performance evaluations, and labeling information for aerosol delivery devices. It is expected that the device is a complete system suitable for its intended use as described in the 510(k) premarket notification. Within the scope of a device application, the applicant should also consult the Intercenter Agreements of October 31, 1991, referenced below for examples of the status of regulated products as devices or drugs. Also note the Intercenter Agreements define that an aerosol delivery device will be considered a drug product and regulated by the Center for Drug Evaluation and Research (CDER), when the primary purpose of the device is delivering or aiding in the delivery of a drug and the device is distributed with the drug. Therefore, if a device is intended to deliver a specific drug or if the labeling references a specific drug product, the device will be considered a drug product and regulated by CDER. It is important to note that Metered Dose Inhalers and Actuators are reviewed in the Center for Drug Evaluation and Research (CDER), where Nebulizers and Spacers as well as Metered Dose Inhalers intended for a ventilator circuit are reviewed in the Center for Devices and Radiological Health (CDRH). Since there are a variety of medical products in the category of nebulizers and MDIS, it is not possible to develop an exhaustive guidance document which will cover all modalities in most applications. However, the general principles regarding the information to be contained in a 510(k) should be valid for all cases.

III. FDA DOCUMENTS

The following documents feature the requirements applicable to 510(K) premarket notification submissions. All of these documents are available from the Division of Small Manufacturers Assistance (DSMA) at 800-638-2041 or 301-443-6597.

(1) Federal Food, Drug, and Cosmetic Act, as Amended, and Related Laws.

(2) Code of Federal Regulations, 21 CFR Parts 50, 56, 8071, 812, and 868.

(3) Premarket Notification: 510 (k) - Regulatory Requirements for Medical Devices (August 1990) (FDA 90-4158).

(4) Investigational Device Exemptions Manual, (June 1992) (FDA 92-4159).

(5) Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (May 29, 1998)

(6) Reviewer Guidance For Premarket Notification Submissions, DCRND/ARDB (November 1993).

(7) ISO 10993-1.

116TH CONGRESS *1st Session* } HOUSE OF REPRESENTATIVES { REPORT 116–47

ORANGE BOOK TRANSPARENCY ACT OF 2019

MAY 2, 2019.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

Mr. PALLONE, from the Committee on Energy and Commerce, submitted the following

R E P O R T

[To accompany H.R. 1503]

[Including cost estimate of the Congressional Budget Office]

The Committee on Energy and Commerce, to whom was referred the bill (H.R. 1503) to amend the Federal Food, Drug, and Cosmetic Act regarding the list under section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act, and for other purposes, having considered the same, report favorably thereon with an amendment and recommend that the bill as amended do pass.

CONTENTS

The amendment is as follows:

Strike all after the enacting clause and insert the following:

89–006

SECTION 1. SHORT TITLE.

This Act may be cited as the "Orange Book Transparency Act of 2019".

SEC. 2. ORANGE BOOK.

(a) SUBMISSION OF PATENT INFORMATION FOR BRAND NAME DRUGS.—Paragraph (1) of section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) is amended to read as follows:

"(b)(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application—

"(A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use;

"(B) a full list of the articles used as components of such drug;

"(C) a full statement of the composition of such drug;

"(D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

"(E) such samples of such drug and of the articles used as components thereof as the Secretary may require;

"(F) specimens of the labeling proposed to be used for such drug;

"(G) any assessments required under section 505B; and

"(H) patent information, with respect to each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug, and consistent with the following requirements:

"(i) The applicant shall file with the application the patent number and the expiration date of—

"(I) any patent which claims the drug for which the applicant submitted the application and is a drug substance (including active ingredient) patent or a drug product (including formulation and composition) patent; and

"(II) any patent which claims the method of using such drug.

"(ii) If an application is filed under this subsection for a drug and a patent of the type described in clause (i) which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include such patent information.

Upon approval of the application, the Secretary shall publish the information submitted under subparagraph (H). The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by subparagraph (A).".

(b) CONFORMING CHANGES TO REQUIREMENTS FOR SUBSEQUENT SUBMISSION OF PATENT INFORMATION.—Section 505(c)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) is amended—

(1) by inserting after "the patent number and the expiration date of any patent which" the following: "fulfills the criteria in subsection (b) and";

(2) by inserting after the first sentence the following: "Patent information that is not the type of patent information required by subsection (b) shall not be submitted."; and

(3) by inserting after "could not file patent information under subsection (b) because no patent" the following: "of the type required to be submitted in subsection (b)".

(c) LISTING OF EXCLUSIVITIES.—Subparagraph (A) of section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) is amended by adding at the end the following:

"(iv) For each drug included on the list, the Secretary shall specify each exclusivity period that is applicable and has not concluded under—

"(I) clause (ii), (iii), or (iv) of subsection (c)(3)(E) of this section;

"(II) clause (iv) or (v) of paragraph (5)(B) of this subsection;

"(III) clause (ii), (iii), or (iv) of paragraph (5)(F) of this subsection;

"(IV) section 505A;

"(V) section 505E; or

"(VI) section 527(a).".

(d) REMOVAL OF INVALID PATENTS.—

(1) IN GENERAL.—Section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) is amended by adding at the end the following:

"(D)(i) The holder of an application approved under subsection (c) for a drug on the list shall notify within 14 days the Secretary in writing if either of the following occurs:

"(I) The Patent Trial and Appeals Board issues a decision from which no appeal has been or can be taken that a patent for such drug is invalid.

"(II) A court issues a decision from which no appeal has been or can be taken that a patent for such drug is invalid.

"(ii) The holder of an approved application shall include in any notification under clause (i) a copy of the decision described in subclause (I) or (II) of clause (i).

"(iii) The Secretary shall remove from the list any patent that is determined to be invalid in a decision described in subclause (I) or (II) of clause (i)—

"(I) promptly; but

"(II) not before the expiration of any 180-day exclusivity period under paragraph (5)(B)(iv) that relies on a certification described in paragraph (2)(A)(vii)(IV) that such patent was invalid.".

(2) APPLICABILITY.—Subparagraph (D) of section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), as added by paragraph (1), applies only with respect to a decision described in such subparagraph that is issued on or after the date of enactment of this Act.

(e) REVIEW AND REPORT.—Not later than one year after the date of enactment of this Act, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall—

(1) solicit public comment regarding the types of patent information that should be included on the list under section 507(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)); and

(2) transmit to the Congress an evaluation of such comments, including any recommendations about the types of patent information that should be included on or removed from such list.

SEC. 3. GAO REPORT TO CONGRESS.

(a) IN GENERAL.—Not later than one year after the date of enactment of this Act, the Comptroller General of the United States (referred to in this section as the "Comptroller General") shall submit to the Committee on Energy and Commerce of the House of Representatives a report on the patents included in the list published under section 505(j)(7) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355(j)(7)), including an analysis and evaluation of the types of patents included in such list and the claims such patents make about the products they claim.

(b) CONTENTS.—The Comptroller General shall include in the report under subsection (a)—

(1) data on the number of—

(A) patents included in the list published under paragraph (7) of section 505(j) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355(j)), that claim the active ingredient or formulation of a drug in combination with a device that is used for delivery of the drug, together comprising the finished dosage form of the drug; and

(B) claims in each patent that claim a device that is used for the delivery of the drug, but do not claim such device in combination with an active ingredient or formulation of a drug;

(2) data on the date of inclusion in the list under paragraph (7) of such section 505(j) for all patents under such list, as compared to patents that claim a method of using the drug in combination with a device;

(3) an analysis regarding the impact of including on the list under paragraph (7) of such section 505(j) certain types of patent information for drug product applicants and approved application holders, including an analysis of whether—

(A) the listing of the patents described in paragraph (1)(A) delayed the market entry of one or more drugs approved under such section 505(j); and

(B) not listing the patents described in paragraph (1)(A) would delay the market entry of one or more such drugs; and

(4) recommendations about which kinds of patents relating to devices described in paragraph (1)(A) should be submitted to the Secretary of Health and Human Services for inclusion on the list under paragraph (7) of such section 505(j) and which patents should not be required to be so submitted.

PURPOSE AND SUMMARY

H.R. 1503, the "Orange Book Transparency Act of 2019", was introduced on March 5, 2019, by Rep. Kelly (D–IL), and referred to the Committee on Energy and Commerce. H.R. 1503 would require manufacturers to share complete and timely patent information with the Food and Drug Administration (FDA), ensure that periods of exclusivity listed in the Orange Book are promptly updated, and

clarify that patents found to be invalid through a court decision or a decision by the Patent Trial and Appeal Board would be required to be removed from the Orange Book promptly, but not before time for appeal has expired. The bill would also direct the U.S. General Accountability Office (GAO) to study which types of patents should be listed in the Orange Book.

Background and Need for Legislation

Approved branded and generic drug products currently marketed are included on a list commonly referred to as the "Orange Book," [1] which is published on the FDA's website and includes, among other details, the patents that protect each product, the product's application number, and some related exclusivities. Drug manufacturers are required to list with FDA patent information related to their drug.[2] This listing in the Orange Book is used by generic manufacturers to make development decisions as it provides information about when patents or exclusivities associated with an approved drug will expire.

While FDA has issued regulations clarifying certain types of patents that must be submitted to the agency and certain types that must not be submitted, many patents are complex and may not fall clearly into the types identified by FDA. As a result, some branded drug manufacturers may choose not to submit every patent on a product to the FDA, and others are submitting patents potentially for the purpose of blocking generic competition.[3] Further, some stakeholders have been critical that the patent information included in the Orange Book is not as accurate or up-to-date as it could be.

This legislation would help to ensure that the Orange Book is accurate and up-to-date, by specifying what information must be submitted to FDA and what information should be listed, clarifying that invalid patents must be removed in a timely manner, directing FDA to solicit public comment on the types of information that should be listed in the Orange Book an evaluation of such comments to Congress, and the GAO to study whether certain patents should, or should not be listed in the Orange Book.

Committee Hearings

For the purposes of section 103(i) of H. Res. 6 of the 116th Congress, the following hearing was used to develop or consider H.R. 1503:

The Subcommittee on Health held a legislative hearing on March 13, 2019, to consider H.R. 1503, the "Orange Book Transparency Act of 2019" and six other bills. The hearing was entitled, "Lowing the Cost of Prescription Drugs: Reducing Barriers to Market Competition." The Subcommittee received testimony from:

- Lou Kennedy, Chief Executive Officer and Owner, Nephron Pharmaceuticals;

---

[1] Food and Drug Administration, *Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)* (https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm).

[2] 21 C.F.R. 314.53

[3] Reed F Bell & Aaron S Kesselheim, *Tertiary patenting on drug—device combination products in the United States,* (https://www.nature.com/articles/nbt.4078.epdf?author_access_token=k19w_aka6yYXhVtkaCGFOdRgN0jAjWel9jnR3ZoTv0MGOAdGITA-e4st1uwIqL0ZGE0-17DL5n2Qg8u7_csdohGlFGwUWdjvieJtiDwzfoldY3_E4HS6rf7YbpkcyvI2u).

- Anthony Barrueta, Senior Vice President for Government Relations, Kaiser Permanente;
- Michael Carrier, Distinguished Professor, Rutgers Law School;
- Kurt Karst, Director, Hyman, Phelps & McNamara, P.C.;
- Jeff Kushan, Partner, Sidley Austin LLP;
- Marc M. Boutin, JD, Chief Executive Officer, National Health Council; and
- Chester "Chip" Davis, Jr., President and Chief Executive Officer, Association for Accessible Medicines.

COMMITTEE CONSIDERATION

H.R. 1503, the "Orange Book Transparency Act of 2019", was introduced on March 5, 2019, by Rep. Kelly (D–IL), and referred to the Committee on Energy and Commerce. The bill was subsequently referred to the Subcommittee on Health on March 6, 2019. Following legislative hearings, the Subcommittee met in open markup session on H.R. 1503 on March 27, 2019, pursuant to notice, for consideration of the bill. A manager's amendment offered by Ms. Kelly was adopted by a voice vote. Subsequently, the Subcommittee on Health agreed to a motion by Ms. Eshoo, Chairwoman of the Subcommittee, to favorably forward H.R. 1503 to the full Committee on Energy and Commerce, amended.

The full Committee on Energy and Commerce met in open markup session, pursuant to notice, on April 3, 2019, to consider H.R. 1503, as amended by the subcommittee. An amendment by Ms. Kelly and Mr. Guthrie was adopted by a voice vote. At the conclusion of consideration and markup of the bill, the Committee agreed to a motion by Mr. Pallone, Chairman of the Committee, to order H.R. 1503 favorably reported to the House, amended, by a voice vote.

COMMITTEE VOTES

Clause 3(b) of rule XIII of the Rules of the House of Representatives requires the Committee to list each record vote on the motion to report legislation and amendments thereto. The Committee advises that there were no record votes taken on H.R. 1503. A motion by Mr. Pallone to order H.R. 1503 favorably reported to the House, amended, was agreed to by a voice vote.

OVERSIGHT FINDINGS

Pursuant to clause 3(c)(1) of rule XIII and clause 2(b)(1) of rule X of the Rules of the House of Representatives, the oversight findings and recommendations of the Committee are reflected in the descriptive portion of the report.

NEW BUDGET AUTHORITY, ENTITLEMENT AUTHORITY, AND TAX EXPENDITURES

Pursuant to 3(c)(2) of rule XIII of the Rules of the House of Representatives, the Committee adopts as its own the estimate of new budget authority, entitlement authority, or tax expenditures or revenues contained in the cost estimate prepared by the Director of

the Congressional Budget Office pursuant to section 402 of the Congressional Budget Act of 1974.

CONGRESSIONAL BUDGET OFFICE ESTIMATE

With respect to the requirements of clause (3)(c)(3) of rule XIII of the Rules of the House of Representatives and section 402 of the Congressional Budget Act of 1974, the Committee has received the following cost estimate for H.R. 1503 from the Director of Congressional Budget Office:

U.S. CONGRESS,
CONGRESSIONAL BUDGET OFFICE,
Washington, DC, May 1, 2019.

Hon. FRANK PALLONE, Jr.,
Chairman, Committee on Energy and Commerce,
House of Representatives, Washington, DC.

DEAR MR. CHAIRMAN: The Congressional Budget Office has prepared the enclosed cost estimate for H.R. 1503, the Orange Book Transparency Act of 2019.

If you wish further details on this estimate, we will be pleased to provide them. The CBO staff contact is Julia Christensen.

Sincerely,

KEITH HALL,
Director.

Enclosure.

H.R. 1503, Orange Book Transparency Act of 2019
As ordered reported by the House Committee on Energy and Commerce on April 3, 2019

By Fiscal Year, Millions of Dollars	2019	2019-2024	2019-2029
Direct Spending (Outlays)	0	0	0
Revenues	0	0	0
Deficit Effect	0	0	0
Spending Subject to Appropriation (Outlays)	0	1	n.e.

Pay-as-you-go procedures apply?	No	Mandate Effects	
Increases on-budget deficits in any of the four consecutive 10-year periods beginning in 2030?	No	Contains intergovernmental mandate?	No
		Contains private-sector mandate?	Yes, Under Threshold

n.e. = not estimated.

Under current law, the Food and Drug Administration (FDA) publishes a compendium entitled, *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly referred to as the "Orange Book." The Orange Book identifies drug products approved on the basis of safety and effectiveness by FDA and provides associated patent and exclusivity information. FDA updates the Orange Book on a regular basis. H.R. 1503 would codify current regulations and practice regarding the types of patent and exclusivity-related information listed in the Orange Book.

H.R. 1503 also would require the prompt removal of certain patents from the Orange Book that have been invalidated by a ruling

of the Patent Trial and Appeal Board at the United States Patent and Trademark Office.

The bill would require FDA to solicit public comments regarding the types of patent information that should be listed in the Orange Book. Within one year of enactment, FDA would be required to transmit to the Congress an evaluation of such comments, including any recommendations about the types of patent information that should be included on or removed from such list.

In addition, H.R. 1503 would direct the General Accountability Office (GAO) to conduct a study that analyzes certain patents with claims relating to devices listed in the Orange Book and evaluates the extent to which listing such patents has affected the timing for the entry of generic drugs into the market. The bill would require GAO to submit the report to the Congress within one year of enactment.

Based on the costs of similar activities, CBO estimates that implementing the bill would cost $1 million, primarily for FDA's personnel-related expenses to comply with the bill's reporting requirements. Any such spending would be subject to the availability of appropriated funds.

H.R. 1503 would impose a private-sector mandate as defined in the Unfunded Mandates Reform Act (UMRA) by requiring drug manufacturers to notify the FDA when the Patent Trial and Appeals Board or another court finds a drug patent to be invalid. CBO estimates the cost of the mandate would fall well below the private-sector threshold established in UMRA ($164 million in 2019, adjusted annually for inflation).

The CBO staff contacts for this estimate are Julia Christensen (for federal costs) and Andrew Laughlin (for mandates). The estimate was reviewed by Leo Lex, Deputy Assistant Director for Budget Analysis.

Federal Mandates Statement

The Committee adopts as its own the estimate of Federal mandates prepared by the Director of the Congressional Budget Office pursuant to section 423 of the Unfunded Mandates Reform Act.

Statement of General Performance Goals and Objectives

Pursuant to clause 3(c)(4) of rule XIII, the general performance goal or objective of this legislation is to amend the Food, Drug, and Cosmetic Act to clarify which patents should be submitted to FDA, that exclusivity periods should be included on the list under 505(j)(7)(A) of the Act, and when invalid patents should be removed from that list. The bill also directs the Comptroller General to conduct a study about the types of patents that are currently included on this list and whether they should continue to be included on this list.

Duplication of Federal Programs

Pursuant to clause 3(c)(5) of rule XIII, no provision of H.R. 1503 is known to be duplicative of another Federal program, including any program that was included in a report to Congress pursuant to section 21 of Public Law 111–139 or the most recent Catalog of Federal Domestic Assistance.

COMMITTEE COST ESTIMATE

Pursuant to clause 3(d)(1) of rule XIII, the Committee adopts as its own the cost estimate prepared by the Director of the Congressional Budget Office pursuant to section 402 of the Congressional Budget Act of 1974.

EARMARKS, LIMITED TAX BENEFITS, AND LIMITED TARIFF BENEFITS

Pursuant to clause 9(e), 9(f), and 9(g) of rule XXI, the Committee finds that H.R. 1503 contains no earmarks, limited tax benefits, or limited tariff benefits.

ADVISORY COMMITTEE STATEMENT

No advisory committees within the meaning of section 5(b) of the Federal Advisory Committee Act were created by this legislation.

APPLICABILITY TO LEGISLATIVE BRANCH

The Committee finds that the legislation does not relate to the terms and conditions of employment or access to public services or accommodations within the meaning of section 102(b)(3) of the Congressional Accountability Act.

SECTION-BY-SECTION ANALYSIS OF THE LEGISLATION

Section 1: Short title

This Act may be cited as the "Orange Book Transparency Act of 2019".

Section 2: Orange Book

Subsection (a) amends section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) to require FDA to include the following patent information for a drug in the Orange Book: drug substance patents, drug product patents, and method of use patents.

Subsection (b) amends the requirements for subsequent submissions of patent information in Section 505(c)(2) to conform to the clarified requirements in 505(b).

Subsection (c) requires the Secretary to specify each exclusivity period for drugs listed in the Orange Book.

Subsection (d) requires that approved drug application holders promptly notify FDA if one of their listed patents is found invalid in a decision from either the Patent Trial and Appeals Board or a court issues a decision from which no appeal has been or can be taken. The legislation further requires that FDA remove a patent from this list promptly if it is found to be invalid, but not before the expiration of any 180-day exclusivity period.

Subsection (e) requires FDA to solicit public comment regarding the types of patent information that should be included on the "Orange Book" and transmit to Congress an evaluation of such comments, including any recommendations about the types of information that should be included or removed from the list.

Section 3: GAO report to Congress

Section 3 directs GAO to analyze and evaluate the types of patents included in the Orange Book and the claims such patents

make about the products they claim, and to include in such analysis specific data and recommendations about the types of patents that should be listed.

CHANGES IN EXISTING LAW MADE BY THE BILL, AS REPORTED

In compliance with clause 3(e) of rule XIII of the Rules of the House of Representatives, changes in existing law made by the bill, as reported, are shown as follows (existing law proposed to be omitted is enclosed in black brackets, new matter is printed in italic, and existing law in which no change is proposed is shown in roman):

FEDERAL FOOD, DRUG, AND COSMETIC ACT

* * * * * * *

CHAPTER V—DRUGS AND DEVICES

SUBCHAPTER A—DRUGS AND DEVICES

* * * * * * *

NEW DRUGS

SEC. 505. (a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug.

(b)[(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, and (G) any assessments required under section 505B. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture use, or sale of the drug. If a application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences. The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appro-

priate, on the inclusion of women and minorities in clinical trials required by clause (A).] *(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application—*

(A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use;

(B) a full list of the articles used as components of such drug;

(C) a full statement of the composition of such drug;

(D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

(E) such samples of such drug and of the articles used as components thereof as the Secretary may require;

(F) specimens of the labeling proposed to be used for such drug;

(G) any assessments required under section 505B; and

(H) patent information, with respect to each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug, and consistent with the following requirements:

(i) The applicant shall file with the application the patent number and the expiration date of—

(I) any patent which claims the drug for which the applicant submitted the application and is a drug substance (including active ingredient) patent or a drug product (including formulation and composition) patent; and

(II) any patent which claims the method of using such drug.

(ii) If an application is filed under this subsection for a drug and a patent of the type described in clause (i) which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include such patent information.

Upon approval of the application, the Secretary shall publish the information submitted under subparagraph (H). The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by subparagraph (A).

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include—

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or

which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c)—

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—

(A) AGREEMENT TO GIVE NOTICE.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give notice as required by this paragraph.

(B) TIMING OF NOTICE.—An applicant that makes a certification described in paragraph (2)(A)(iv) shall give notice as required under this paragraph—

(i) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(ii) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(C) RECIPIENTS OF NOTICE.—An applicant required under this paragraph to give notice shall give notice to—

(i) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(ii) the holder of the approved application under this subsection for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(D) CONTENTS OF NOTICE.—A notice required under this paragraph shall—

(i) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(ii) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(4)(A) An applicant may not amend or supplement an application referred to in paragraph (2) to seek approval of a drug that is a different drug than the drug identified in the application as submitted to the Secretary.

(B) With respect to the drug for which such an application is submitted, nothing in this subsection or subsection (c)(3) prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(5)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1) or under section 351 of the Public Health Service Act, which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection or section 351 of the Public Health Service Act if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size—

(i)(I) of clinical trials intended to form the primary basis of an effectiveness claim; or

(II) in the case where human efficacy studies are not ethical or feasible, of animal and any associated clinical trials which, in combination, are intended to form the primary basis of an effectiveness claim; or

(ii) with respect to an application for approval of a biological product under section 351(k) of the Public Health Service Act, of any necessary clinical study or studies.

The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of the clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

(C) Any agreement regarding the parameters of the design and size of clinical trials of a new drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection or section 351 of the Public Health Service Act (including all scientific and medical matters, chemistry, manufacturing, and controls).

(6) An application submitted under this subsection shall be accompanied by the certification required under section 402(j)(5)(B) of the Public Health Service Act. Such certification shall not be considered an element of such application.

(c)(1) Within one hundred and eighty days after the filing of an application under subsection (b), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

(A) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) applies, or

(B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) If the patent information described in subsection (b) could not be filed with the submission of an application under subsection (b) because the application was filed before the patent information was required under subsection (b) or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary, the patent number and the expiration date of any patent which *fulfills the criteria in subsection (b) and* claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. *Patent information that is not the type of patent information required by subsection (b) shall not be submitted.* If the holder of an approved application could not file patent information under subsection (b) because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after the date of the enactment of this sentence, and if the holder of an approved application could not file patent information

under subsection (b) because no patent *of the type required to be submitted in subsection (b)* had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(3) The approval of an application filed under subsection (b) which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined by applying the following to each certification made under subsection (b)(2)(A):

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A), the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under paragraph (2) or subsection (b)(1) before the date on which the application (excluding an amendment or supplement to the application) was submitted. If such an action is brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under subsection (b)(3) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(i) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(I) the date on which the court enters judgment reflecting the decision; or

(II) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(ii) if before the expiration of such period the district court decides that the patent has been infringed—

(I) if the judgment of the district court is appealed, the approval shall be made effective on—

(aa) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity); or

(bb) the date of a settlement order or consent decree signed and entered by the court of appeals

stating that the patent that is the subject of the certification is invalid or not infringed; or

(II) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35, United States Code;

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in clause (i); or

(iv) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in clause (ii).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(D) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.—

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.—

(I) IN GENERAL.—No action may be brought under section 2201 of title 28, United States Code, by an applicant referred to in subsection (b)(2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (C) unless—

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) FILING OF CIVIL ACTION.—If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, United States Code, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the

patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant referred to in subsection (b)(2) for the purpose of determining whether an action referred to in subparagraph (C) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under subsection (b)(2)(A)(iv) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.—

(I) IN GENERAL.—If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or this subsection on the ground that the patent does not claim either—

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) NO INDEPENDENT CAUSE OF ACTION.—Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) NO DAMAGES.—An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(E)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), was approved during the period beginning January 1, 1982, and ending on the date of the enactment of this subsection, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b).

(ii) If an application submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), is approved after the date of the enactment of this clause, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under subsection (b) after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A). The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b), is approved after the date of the enactment of this clause and if such appli-

cation contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) if the investigations described in clause (A) of subsection (b)(1) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) is approved after the date of enactment of this clause and the supplement contains reports of new clinical investigations (other than bioavailabilty studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) if the investigations described in clause (A) of subsection (b)(1) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on the date of the enactment of this clause, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from the date of enactment of this clause.

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval for the drug prior to manufacture of the drug in a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(5)(A) The Secretary may rely upon qualified data summaries to support the approval of a supplemental application, with respect to a qualified indication for a drug, submitted under subsection (b), if such supplemental application complies with subparagraph (B).

(B) A supplemental application is eligible for review as described in subparagraph (A) only if—

(i) there is existing data available and acceptable to the Secretary demonstrating the safety of the drug; and

(ii) all data used to develop the qualified data summaries are submitted to the Secretary as part of the supplemental application.

(C) The Secretary shall post on the Internet website of the Food and Drug Administration and update annually—

(i) the number of applications reviewed solely under subparagraph (A) or section 351(a)(2)(E) of the Public Health Service Act;

(ii) the average time for completion of review under subparagraph (A) or section 351(a)(2)(E) of the Public Health Service Act;

(iii) the average time for review of supplemental applications where the Secretary did not use review flexibility under subparagraph (A) or section 351(a)(2)(E) of the Public Health Service Act; and

(iv) the number of applications reviewed under subparagraph (A) or section 351(a)(2)(E) of the Public Health Service Act for which the Secretary made use of full data sets in addition to the qualified data summary.

(D) In this paragraph—

(i) the term "qualified indication" means an indication for a drug that the Secretary determines to be appropriate for summary level review under this paragraph; and

(ii) the term "qualified data summary" means a summary of clinical data that demonstrates the safety and effectiveness of a drug with respect to a qualified indication.

(d) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is

false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e), the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence. The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decisionmaking, and the communication of the benefits and risks of new drugs. Nothing in the preceding sentence shall alter the criteria for evaluating an application for marketing approval of a drug.

(e) The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided,* That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The

Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) or to comply with the notice requirements of section 510(k)(2), or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based. The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an assessment of the approved risk evaluation and mitigation strategy for the drug under section 505–1(g)(2)(D).

(f) Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

(g) Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the Department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

(h) An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of title 28, United States Code. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the

record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of title 28 of the United States Code. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

(i)(1) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(A) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, or preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

(B) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings;

(C) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b); and

(D) the submission to the Secretary by the manufacturer or the sponsor of the investigation of a new drug of a statement of intent regarding whether the manufacturer or

sponsor has plans for assessing pediatric safety and efficacy.

(2) Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including—

(A) information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and

(B) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.

(3)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a "clinical hold") if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that—

(i) the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before the date of the enactment of the Food and Drug Administration Modernization Act of 1997).

(C) Any written request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible, it is contrary to the best interests of such human beings, or the proposed clinical testing poses no more than minimal risk to such human beings and includes appropriate safeguards as prescribed to protect the rights, safety, and welfare of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs. The Secretary shall update such regula-

tions to require inclusion in the informed consent documents and process a statement that clinical trial information for such clinical investigation has been or will be submitted for inclusion in the registry data bank pursuant to subsection (j) of section 402 of the Public Health Service Act.

(j)(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain—

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (7) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 201(p), and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (B) through (F) of subsection (b)(1);

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c)—

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B) NOTICE OF OPINION THAT PATENT IS INVALID OR WILL NOT BE INFRINGED.—

(i) AGREEMENT TO GIVE NOTICE.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give notice as required by this subparagraph.

(ii) TIMING OF NOTICE.—An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph—

(I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed; or

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

(iii) RECIPIENTS OF NOTICE.—An applicant required under this subparagraph to give notice shall give notice to—

(I) each owner of the patent that is the subject of the certification (or a representative of the owner designated to receive such a notice); and

(II) the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent (or a representative of the holder designated to receive such a notice).

(iv) CONTENTS OF NOTICE.—A notice required under this subparagraph shall—

(I) state that an application that contains data from bioavailability or bioequivalence studies has been submitted under this subsection for the drug with respect to which

the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification; and

(II) include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds—

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(D)(i) An applicant may not amend or supplement an application to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary.

(ii) With respect to the drug for which an application is submitted, nothing in this subsection prohibits an applicant from amending or supplementing the application to seek approval of a different strength.

(iii) Within 60 days after the date of the enactment of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, the Secretary shall issue guidance defining the term "listed drug" for purposes of this subparagraph.

(3)(A) The Secretary shall issue guidance for the individuals who review applications submitted under paragraph (1), which shall relate to promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards, and which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval for a drug under this subsection if the sponsor or applicant makes a reasonable written request for a meeting for the purpose of reaching agreement on the design and size of bioavailability and bioequivalence studies needed for approval of such application. The sponsor or applicant shall provide information necessary for discussion and agreement on the design and size of such studies. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

(C) Any agreement regarding the parameters of design and size of bioavailability and bioequivalence studies of a drug under this paragraph that is reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the admin-

istrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

(i) with the written agreement of the sponsor or applicant; or

(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the reviewing division, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director will document the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified.

(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

(G) For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug under this subsection (including scientific matters, chemistry, manufacturing, and controls).

(4) Subject to paragraph (5), the Secretary shall approve an application for a drug unless the Secretary finds—

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show—

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 201(p),

or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type or quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e), the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) for grounds described in the first sentence of subsection (e), the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (6), or the Sec-

retary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirement of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the district court decides that the patent is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), the approval shall be made effective on—

(aa) the date on which the court enters judgment reflecting the decision; or

(bb) the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed;

(II) if before the expiration of such period the district court decides that the patent has been infringed—

(aa) if the judgment of the district court is appealed, the approval shall be made effective on—

(AA) the date on which the court of appeals decides that the patent is invalid or not infringed (including any substantive determination that

there is no cause of action for patent infringement or invalidity); or

(BB) the date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent that is the subject of the certification is invalid or not infringed; or

(bb) if the judgment of the district court is not appealed or is affirmed, the approval shall be made effective on the date specified by the district court in a court order under section 271(e)(4)(A) of title 35, United States Code;

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective as provided in subclause (I); or

(IV) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent has been infringed, the approval shall be made effective as provided in subclause (II).

In such an action, each of the parties shall reasonably cooperate in expediting the action.

(iv) 180-DAY EXCLUSIVITY PERIOD.—

(I) EFFECTIVENESS OF APPLICATION.—Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

(II) DEFINITIONS.—In this paragraph:

(aa) 180-DAY EXCLUSIVITY PERIOD.—The term "180-day exclusivity period" means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

(bb) FIRST APPLICANT.—As used in this subsection, the term "first applicant" means an applicant that, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug.

(cc) SUBSTANTIALLY COMPLETE APPLICATION.—As used in this subsection, the term "substantially complete application" means an application under this subsection that on its face is sufficiently complete to

permit a substantive review and contains all the information required by paragraph (2)(A).

(dd) TENTATIVE APPROVAL.—

(AA) IN GENERAL.—The term "tentative approval" means notification to an applicant by the Secretary that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the application does not meet the requirements of this subparagraph, there is a period of exclusivity for the listed drug under subparagraph (F) or section 505A, or there is a 7-year period of exclusivity for the listed drug under section 527.

(BB) LIMITATION.—A drug that is granted tentative approval by the Secretary is not an approved drug and shall not have an effective approval until the Secretary issues an approval after any necessary additional review of the application.

(v) 180-DAY EXCLUSIVITY PERIOD FOR COMPETITIVE GENERIC THERAPIES.—

(I) EFFECTIVENESS OF APPLICATION.—Subject to subparagraph (D)(iv), if the application is for a drug that is the same as a competitive generic therapy for which any first approved applicant has commenced commercial marketing, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the competitive generic therapy (including the commercial marketing of the listed drug) by any first approved applicant.

(II) LIMITATION.—The exclusivity period under subclause (I) shall not apply with respect to a competitive generic therapy that has previously received an exclusivity period under subclause (I).

(III) DEFINITIONS.—In this clause and subparagraph (D)(iv):

(aa) The term "competitive generic therapy" means a drug—

(AA) that is designated as a competitive generic therapy under section 506H; and

(BB) for which there are no unexpired patents or exclusivities on the list of products described in section 505(j)(7)(A) at the time of submission.

(bb) The term "first approved applicant" means any applicant that has submitted an application that—

(AA) is for a competitive generic therapy that is approved on the first day on which any application for such competitive generic therapy is approved;

(BB) is not eligible for a 180-day exclusivity period under clause (iv) for the drug that is the subject of the application for the competitive generic therapy; and

(CC) is not for a drug for which all drug versions have forfeited eligibility for a 180-day ex-

clusivity period under clause (iv) pursuant to subparagraph (D).

(C) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.—

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.—

(I) IN GENERAL.—No action may be brought under section 2201 of title 28, United States Code, by an applicant under paragraph (2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (B)(iii) unless—

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to noninfringement, the notice was accompanied by a document described in subclause (III).

(II) FILING OF CIVIL ACTION.—If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, United States Code, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice) for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.—For purposes of subclause (I)(cc), the document described in this subclause is a document providing an offer of confidential access to the application that is in the custody of the applicant under paragraph (2) for the purpose of determining whether an action referred to in subparagraph (B)(iii) should be brought. The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and

other confidential business information. A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract. Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement.

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.—

(I) IN GENERAL.—If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) on the ground that the patent does not claim either—

(aa) the drug for which the application was approved; or

(bb) an approved method of using the drug.

(II) NO INDEPENDENT CAUSE OF ACTION.—Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) NO DAMAGES.—An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

(D) FORFEITURE OF 180-DAY EXCLUSIVITY PERIOD.—

(i) DEFINITION OF FORFEITURE EVENT.—In this subparagraph, the term "forfeiture event", with respect to an application under this subsection, means the occurrence of any of the following:

(I) FAILURE TO MARKET.—The first applicant fails to market the drug by the later of—

(aa) the earlier of the date that is—

(AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or

(BB) 30 months after the date of submission of the application of the first applicant; or

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).

(II) WITHDRAWAL OF APPLICATION.—The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) AMENDMENT OF CERTIFICATION.—The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) FAILURE TO OBTAIN TENTATIVE APPROVAL.—The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) AGREEMENT WITH ANOTHER APPLICANT, THE LISTED DRUG APPLICATION HOLDER, OR A PATENT OWNER.—The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal

Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 1 of the Clayton Act (15 U.S.C. 12), except that the term includes section 5 of the Federal Trade Commission Act (15 U.S.C. 45) to the extent that that section applies to unfair methods of competition).

(VI) EXPIRATION OF ALL PATENTS.—All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

(ii) FORFEITURE.—The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) SUBSEQUENT APPLICANT.—If all first applicants forfeit the 180-day exclusivity period under clause (ii)—

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

(iv) SPECIAL FORFEITURE RULE FOR COMPETITIVE GENERIC THERAPY.—The 180-day exclusivity period described in subparagraph (B)(v) shall be forfeited by a first approved applicant if the applicant fails to market the competitive generic therapy within 75 days after the date on which the approval of the first approved applicant's application for the competitive generic therapy is made effective.

(E) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(F)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), was approved during the period beginning January 1, 1982, and ending on the date of the enactment of this subsection, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b).

(ii) If an application submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), is approved after the date of the enactment of this subsection, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b), except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b), is approved after the date of enactment of this subsection and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) for such drug.

(iv) If a supplement to an application approved under subsection (b) is approved after the date of enactment of this subsection and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b).

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b), was approved during the period beginning January 1, 1982, and ending on the date of the enactment of this subsection, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b) application effective before the expiration of two years from the date of enactment of this subsection.

(6) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn

or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended—

(A) for the same period as the withdrawal or suspension under subsection (e) or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(7)(A)(i) Within sixty days of the date of the enactment of this subsection, the Secretary shall publish and make available to the public—

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) before the date of the enactment of this subsection;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (b) or (c) respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(iv) For each drug included on the list, the Secretary shall specify each exclusivity period that is applicable and has not concluded under—

(I) clause (ii), (iii), or (iv) of subsection (c)(3)(E) of this section;

(II) clause (iv) or (v) of paragraph (5)(B) of this subsection;

(III) clause (ii), (iii), or (iv) of paragraph (5)(F) of this subsection;

(IV) section 505A;

(V) section 505E; or

(VI) section 527(a).

(B) A drug approved for safety and effectiveness under subsection (c) or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or the date of enactment, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under paragraph (6) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its

publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (e) or paragraph (6), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(D)(i) The holder of an application approved under subsection (c) for a drug on the list shall notify within 14 days the Secretary in writing if either of the following occurs:

(I) The Patent Trial and Appeals Board issues a decision from which no appeal has been or can be taken that a patent for such drug is invalid.

(II) A court issues a decision from which no appeal has been or can be taken that a patent for such drug is invalid.

(ii) The holder of an approved application shall include in any notification under clause (i) a copy of the decision described in subclause (I) or (II) of clause (i).

(iii) The Secretary shall remove from the list any patent that is determined to be invalid in a decision described in subclause (I) or (II) of clause (i)—

(I) promptly; but

(II) not before the expiration of any 180-day exclusivity period under paragraph (5)(B)(iv) that relies on a certification described in paragraph (2)(A)(vii)(IV) that such patent was invalid.

(8) For purposes of this subsection:

(A)(i) The term "bioavailability" means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(ii) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may assess bioavailability by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or therapeutic ingredient becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if—

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug

concentrations on chronic use, and is considered medically insignificant for the drug.

(C) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect.

(9) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of—

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(10)(A) If the proposed labeling of a drug that is the subject of an application under this subsection differs from the listed drug due to a labeling revision described under clause (i), the drug that is the subject of such application shall, notwithstanding any other provision of this Act, be eligible for approval and shall not be considered misbranded under section 502 if—

(i) the application is otherwise eligible for approval under this subsection but for expiration of patent, an exclusivity period, or of a delay in approval described in paragraph (5)(B)(iii), and a revision to the labeling of the listed drug has been approved by the Secretary within 60 days of such expiration;

(ii) the labeling revision described under clause (i) does not include a change to the "Warnings" section of the labeling;

(iii) the sponsor of the application under this subsection agrees to submit revised labeling of the drug that is the subject of such application not later than 60 days after the notification of any changes to such labeling required by the Secretary; and

(iv) such application otherwise meets the applicable requirements for approval under this subsection.

(B) If, after a labeling revision described in subparagraph (A)(i), the Secretary determines that the continued presence in interstate commerce of the labeling of the listed drug (as in effect before the revision described in subparagraph (A)(i)) adversely impacts the safe use of the drug, no application under this subsection shall be eligible for approval with such labeling.

(11)(A) Subject to subparagraph (B), the Secretary shall prioritize the review of, and act within 8 months of the date of the submission of, an original abbreviated new drug application submitted for review under this subsection that is for a drug—

(i) for which there are not more than 3 approved drug products listed under paragraph (7) and for which there are no blocking patents and exclusivities; or

(ii) that has been included on the list under section 506E.

(B) To qualify for priority review under this paragraph, not later than 60 days prior to the submission of an application described in subparagraph (A) or that the Secretary may prioritize pursuant to subparagraph (D), the applicant shall provide complete, accurate information regarding facilities involved in manufacturing processes and testing of the drug that is the subject of the application, including facilities in corresponding Type II active pharmaceutical ingredients drug master files referenced in an application and sites or organizations involved in bioequivalence and clinical studies used to support the application, to enable the Secretary to make a determination regarding whether an inspection of a facility is necessary. Such information shall include the relevant (as determined by the Secretary) sections of such application, which shall be unchanged relative to the date of the submission of such application, except to the extent that a change is made to such information to exclude a facility that was not used to generate data to meet any application requirements for such submission and that is not the only facility intended to conduct one or more unit operations in commercial production. Information provided by an applicant under this subparagraph shall not be considered the submission of an application under this subsection.

(C) The Secretary may expedite an inspection or reinspection under section 704 of an establishment that proposes to manufacture a drug described in subparagraph (A).

(D) Nothing in this paragraph shall prevent the Secretary from prioritizing the review of other applications as the Secretary determines appropriate.

(12) The Secretary shall publish on the internet website of the Food and Drug Administration, and update at least once every 6 months, a list of all drugs approved under subsection (c) for which all patents and periods of exclusivity under this Act have expired and for which no application has been approved under this subsection.

(13) Upon the request of an applicant regarding one or more specified pending applications under this subsection, the Secretary shall, as appropriate, provide review status updates indicating the categorical status of the applications by each relevant review discipline.

(k)(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section. Regulations and orders issued under this subsection and under subsection (i) shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(3) ACTIVE POSTMARKET RISK IDENTIFICATION.—

(A) DEFINITION.—In this paragraph, the term "data" refers to information with respect to a drug approved under this section or under section 351 of the Public Health Service Act, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

(B) DEVELOPMENT OF POSTMARKET RISK IDENTIFICATION AND ANALYSIS METHODS.—The Secretary shall, not later than 2 years after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, in collaboration with public, academic, and private entities—

(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate—

(I) at least 25,000,000 patients by July 1, 2010; and

(II) at least 100,000,000 patients by July 1, 2012; and

(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

(C) ESTABLISHMENT OF THE POSTMARKET RISK IDENTIFICATION AND ANALYSIS SYSTEM.—

(i) IN GENERAL.—The Secretary shall, not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), establish and maintain procedures—

(I) for risk identification and analysis based on electronic health data, in compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996, and in a manner that does not disclose individually identifiable health information in violation of paragraph (4)(B);

(II) for the reporting (in a standardized form) of data on all serious adverse drug experiences (as defined in section 505–1(b)) submitted to the Secretary under paragraph (1), and those adverse

events submitted by patients, providers, and drug sponsors, when appropriate;

(III) to provide for active adverse event surveillance using the following data sources, as available:

(aa) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

(bb) private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data); and

(cc) other data as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

(IV) to identify certain trends and patterns with respect to data accessed by the system;

(V) to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, and other information the Secretary determines appropriate, which may include data on comparative national adverse event trends; and

(VI) to enable the program to export data in a form appropriate for further aggregation, statistical analysis, and reporting.

(ii) TIMELINESS OF REPORTING.—The procedures established under clause (i) shall ensure that such data are accessed, analyzed, and reported in a timely, routine, and systematic manner, taking into consideration the need for data completeness, coding, cleansing, and standardized analysis and transmission.

(iii) PRIVATE SECTOR RESOURCES.—To ensure the establishment of the active postmarket risk identification and analysis system under this subsection not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), as required under clause (i), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(iv) COMPLEMENTARY APPROACHES.—To the extent the active postmarket risk identification and analysis system under this subsection is not sufficient to gather data and information relevant to a priority drug safety question, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including—

(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

(v) AUTHORITY FOR CONTRACTS.—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

(4) ADVANCED ANALYSIS OF DRUG SAFETY DATA.—

(A) PURPOSE.—The Secretary shall establish collaborations with public, academic, and private entities, which may include the Centers for Education and Research on Therapeutics under section 912 of the Public Health Service Act, to provide for advanced analysis of drug safety data described in paragraph (3)(C) and other information that is publicly available or is provided by the Secretary, in order to—

(i) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

(ii) provide the Secretary with routine access to outside expertise to study advanced drug safety questions; and

(iii) enhance the ability of the Secretary to make timely assessments based on drug safety data.

(B) PRIVACY.—Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals and trends or when responding to inquiries regarding such drug safety signals and trends.

(C) PUBLIC PROCESS FOR PRIORITY QUESTIONS.—At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or any successor committee) and from other advisory committees, as appropriate, to the Food and Drug Administration on—

(i) priority drug safety questions; and

(ii) mechanisms for answering such questions, including through—

(I) active risk identification under paragraph (3); and

(II) when such risk identification is not sufficient, postapproval studies and clinical trials under subsection (o)(3).

(D) PROCEDURES FOR THE DEVELOPMENT OF DRUG SAFETY COLLABORATIONS.—

(i) IN GENERAL.—Not later than 180 days after the date of the establishment of the active postmarket risk identification and analysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to—

(I) classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary;

(II) allow for prompt investigation of priority drug safety questions, including—

(aa) unresolved safety questions for drugs or classes of drugs; and

(bb) for a newly-approved drugs, safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children);

(III) perform advanced research and analysis on identified drug safety risks;

(IV) focus postapproval studies and clinical trials under subsection (o)(3) more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious adverse event associated with the use of a drug; and

(V) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

(ii) REQUEST FOR SPECIFIC METHODOLOGY.—The procedures described in clause (i) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

(E) USE OF ANALYSES.—The Secretary shall provide the analyses described in this paragraph, including the methods and results of such analyses, about a drug to the sponsor or sponsors of such drug.

(F) QUALIFIED ENTITIES.—

(i) IN GENERAL.—The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide information to the Secretary in a timely manner.

(ii) QUALIFICATION.—The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

(I) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

(II) An information technology infrastructure in place to support electronic data and operational standards to provide security for such data.

(III) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

(IV) An understanding of drug development or risk/benefit balancing in a clinical setting.

(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

(G) CONTRACT REQUIREMENTS.—Each contract with a qualified entity under subparagraph (F)(i) shall contain the following requirements:

(i) ENSURING PRIVACY.—The qualified entity shall ensure that the entity will not use data under this subsection in a manner that—

(I) violates the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996;

(II) violates sections 552 or 552a of title 5, United States Code, with regard to the privacy of individually-identifiable beneficiary health information; or

(III) discloses individually identifiable health information when presenting drug safety signals and trends or when responding to inquiries regarding drug safety signals and trends.

Nothing in this clause prohibits lawful disclosure for other purposes.

(ii) COMPONENT OF ANOTHER ORGANIZATION.—If a qualified entity is a component of another organization—

(I) the qualified entity shall establish appropriate security measures to maintain the confidentiality and privacy of such data; and

(II) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

(iii) TERMINATION OR NONRENEWAL.—If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

(I) CONFIDENTIALITY AND PRIVACY PROTECTIONS.—The entity shall continue to comply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

(II) DISPOSITION OF DATA.—The entity shall return any data disclosed to such entity under this subsection to which it would not otherwise have access or, if returning the data is not practicable, destroy the data.

(H) COMPETITIVE PROCEDURES.—The Secretary shall use competitive procedures (as defined in section 4(5) of the Federal Procurement Policy Act) to enter into contracts under subparagraph (G).

(I) REVIEW OF CONTRACT IN THE EVENT OF A MERGER OR ACQUISITION.—The Secretary shall review the contract with a qualified entity under this paragraph in the event of a merger or acquisition of the entity in order to ensure

that the requirements under this paragraph will continue to be met.

(J) COORDINATION.—In carrying out this paragraph, the Secretary shall provide for appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and to the extent practicable shall coordinate with the activities of private entities, professional associations, or other entities that may have sources of drug safety data.

(5) The Secretary shall—

(A) conduct regular screenings of the Adverse Event Reporting System database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by Adverse Event Reporting System within the last quarter; and

(B) on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments; and

(C) make available on the Internet website of the Food and Drug Administration—

(i) guidelines, developed with input from experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, that detail best practices for drug safety surveillance using the Adverse Event Reporting System; and

(ii) criteria for public posting of adverse event signals.

(l)(1) Safety and effectiveness data and information which has been submitted in an application under subsection (b) for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown—

(A) if no work is being or will be undertaken to have the application approved,

(B) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(C) if approval of the application under subsection (c) is withdrawn and all legal appeals have been exhausted,

(D) if the Secretary has determined that such drug is not a new drug, or

(E) upon the effective date of the approval of the first application under subsection (j) which refers to such drug or upon the date upon which the approval of an application under subsection (j) which refers to such drug could be made effective if such an application had been submitted.

(2) ACTION PACKAGE FOR APPROVAL.—

(A) ACTION PACKAGE.—The Secretary shall publish the action package for approval of an application under subsection (b) or section 351 of the Public Health Service Act on the Internet Web site of the Food and Drug Administration—

(i) not later than 30 days after the date of approval of such application for a drug no active ingredient (including

any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 351 of the Public Health Service Act; and

(ii) not later than 30 days after the third request for such action package for approval received under section 552 of title 5, United States Code, for any other drug.

(B) IMMEDIATE PUBLICATION OF SUMMARY REVIEW.—Notwithstanding subparagraph (A), the Secretary shall publish, on the Internet Web site of the Food and Drug Administration, the materials described in subparagraph (C)(iv) not later than 48 hours after the date of approval of the drug, except where such materials require redaction by the Secretary.

(C) CONTENTS.—An action package for approval of an application under subparagraph (A) shall be dated and shall include the following:

(i) Documents generated by the Food and Drug Administration related to review of the application.

(ii) Documents pertaining to the format and content of the application generated during drug development.

(iii) Labeling submitted by the applicant.

(iv) A summary review that documents conclusions from all reviewing disciplines about the drug, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrence with review conclusions.

(v) The Division Director and Office Director's decision document which includes—

(I) a brief statement of concurrence with the summary review;

(II) a separate review or addendum to the review if disagreeing with the summary review; and

(III) a separate review or addendum to the review to add further analysis.

(vi) Identification by name of each officer or employee of the Food and Drug Administration who—

(I) participated in the decision to approve the application; and

(II) consents to have his or her name included in the package.

(D) REVIEW.—A scientific review of an application is considered the work of the reviewer and shall not be altered by management or the reviewer once final.

(E) CONFIDENTIAL INFORMATION.—This paragraph does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of title 5, United States Code.

(m) For purposes of this section, the term "patent" means a patent issued by the United States Patent and Trademark Office.

(n)(1) For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under section 505 or section 351 of the Public Health Service Act, the Secretary shall establish panels of experts or use panels of experts established be-

fore the date of enactment of the Food and Drug Administration Modernization Act of 1997, or both.

(2) The Secretary may delegate the appointment and oversight authority granted under section 1004 to a director of a center or successor entity within the Food and Drug Administration.

(3) The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of—

(A) members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

(B) members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoeconomics, biological and physical sciences, and other related professions;

(C) a representative of consumer interests, and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

(D) two or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this Act may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(4) The Secretary shall, as appropriate, provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this Act and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

(5) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS–15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, United States Code, for persons in the Government service employed intermittently.

(6) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

(7) Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the

conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

(o) POSTMARKET STUDIES AND CLINICAL TRIALS; LABELING.—

(1) IN GENERAL.—A responsible person may not introduce or deliver for introduction into interstate commerce the new drug involved if the person is in violation of a requirement established under paragraph (3) or (4) with respect to the drug.

(2) DEFINITIONS.—For purposes of this subsection:

(A) RESPONSIBLE PERSON.—The term "responsible person" means a person who—

(i) has submitted to the Secretary a covered application that is pending; or

(ii) is the holder of an approved covered application.

(B) COVERED APPLICATION.—The term "covered application" means—

(i) an application under subsection (b) for a drug that is subject to section 503(b); and

(ii) an application under section 351 of the Public Health Service Act.

(C) NEW SAFETY INFORMATION; SERIOUS RISK.—The terms "new safety information", "serious risk", and "signal of a serious risk" have the meanings given such terms in section 505–1(b).

(3) STUDIES AND CLINICAL TRIALS.—

(A) IN GENERAL.—For any or all of the purposes specified in subparagraph (B), the Secretary may, subject to subparagraph (D), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific data deemed appropriate by the Secretary, including information regarding chemically-related or pharmacologically-related drugs.

(B) PURPOSES OF STUDY OR CLINICAL TRIAL.—The purposes referred to in this subparagraph with respect to a postapproval study or postapproval clinical trial are the following:

(i) To assess a known serious risk related to the use of the drug involved.

(ii) To assess signals of serious risk related to the use of the drug.

(iii) To identify an unexpected serious risk when available data indicates the potential for a serious risk.

(C) ESTABLISHMENT OF REQUIREMENT AFTER APPROVAL OF COVERED APPLICATION.—The Secretary may require a postapproval study or studies or postapproval clinical trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information.

(D) DETERMINATION BY SECRETARY.—

(i) POSTAPPROVAL STUDIES.—The Secretary may not require the responsible person to conduct a study

under this paragraph, unless the Secretary makes a determination that the reports under subsection (k)(1) and the active postmarket risk identification and analysis system as available under subsection (k)(3) will not be sufficient to meet the purposes set forth in subparagraph (B).

(ii) POSTAPPROVAL CLINICAL TRIALS.—The Secretary may not require the responsible person to conduct a clinical trial under this paragraph, unless the Secretary makes a determination that a postapproval study or studies will not be sufficient to meet the purposes set forth in subparagraph (B).

(E) NOTIFICATION; TIMETABLES; PERIODIC REPORTS.—

(i) NOTIFICATION.—The Secretary shall notify the responsible person regarding a requirement under this paragraph to conduct a postapproval study or clinical trial by the target dates for communication of feedback from the review team to the responsible person regarding proposed labeling and postmarketing study commitments as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

(ii) TIMETABLE; PERIODIC REPORTS.—For each study or clinical trial required to be conducted under this paragraph, the Secretary shall require that the responsible person submit a timetable for completion of the study or clinical trial. With respect to each study required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such study including whether any difficulties in completing the study have been encountered. With respect to each clinical trial required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such clinical trial including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to the requirements under section 402(j) of the Public Health Service Act. If the responsible person fails to comply with such timetable or violates any other requirement of this subparagraph, the responsible person shall be considered in violation of this subsection, unless the responsible person demonstrates good cause for such noncompliance or such other violation. The Secretary shall determine what constitutes good cause under the preceding sentence.

(F) DISPUTE RESOLUTION.—The responsible person may appeal a requirement to conduct a study or clinical trial

under this paragraph using dispute resolution procedures established by the Secretary in regulation and guidance.

(4) SAFETY LABELING CHANGES REQUESTED BY SECRETARY.—

(A) NEW SAFETY OR NEW EFFECTIVENESS INFORMATION.—If the Secretary becomes aware of new information, including any new safety information or information related to reduced effectiveness, that the Secretary determines should be included in the labeling of the drug, the Secretary shall promptly notify the responsible person or, if the same drug approved under section 505(b) is not currently marketed, the holder of an approved application under 505(j).

(B) RESPONSE TO NOTIFICATION.—Following notification pursuant to subparagraph (A), the responsible person or the holder of the approved application under section 505(j) shall within 30 days—

(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions, or new effectiveness information; or

(ii) notify the Secretary that the responsible person or the holder of the approved application under section 505(j) does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

(C) REVIEW.—Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the reasons why no labeling change is necessary, the Secretary shall initiate discussions to reach agreement on whether the labeling for the drug should be modified to reflect the new safety or new effectiveness information, and if so, the contents of such labeling changes.

(D) DISCUSSIONS.—Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

(E) ORDER.—Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person or the holder of the approved application under section 505(j) to make such a labeling change as the Secretary deems appropriate to address the new safety or new effectiveness information. Within 15 days of such an order, the responsible person or the holder of the approved application under section 505(j) shall submit a supplement containing the labeling change.

(F) DISPUTE RESOLUTION.—Within 5 days of receiving an order under subparagraph (E), the responsible person or the holder of the approved application under section 505(j) may appeal using dispute resolution procedures established by the Secretary in regulation and guidance.

(G) VIOLATION.—If the responsible person or the holder of the approved application under section 505(j) has not

submitted a supplement within 15 days of the date of such order under subparagraph (E), and there is no appeal or dispute resolution proceeding pending, the responsible person or holder shall be considered to be in violation of this subsection. If at the conclusion of any dispute resolution procedures the Secretary determines that a supplement must be submitted and such a supplement is not submitted within 15 days of the date of that determination, the responsible person or holder shall be in violation of this subsection.

(H) PUBLIC HEALTH THREAT.—Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that such a labeling change is necessary to protect the public health, the Secretary may accelerate the timelines in such subparagraphs.

(I) RULE OF CONSTRUCTION.—This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under section 505(j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).

(5) NON-DELEGATION.—Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

(p) RISK EVALUATION AND MITIGATION STRATEGY.—

(1) IN GENERAL.—A person may not introduce or deliver for introduction into interstate commerce a new drug if—

(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 503(b); or

(ii) the application for such drug is approved under section 351 of the Public Health Service Act; and

(B) a risk evaluation and mitigation strategy is required under section 505–1 with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 505–1, including requirements regarding assessments of approved strategies.

(2) CERTAIN POSTMARKET STUDIES.—The failure to conduct a postmarket study under section 506, subpart H of part 314, or subpart E of part 601 of title 21, Code of Federal Regulations (or any successor regulations), is deemed to be a violation of paragraph (1).

(q) PETITIONS AND CIVIL ACTIONS REGARDING APPROVAL OF CERTAIN APPLICATIONS.—

(1) IN GENERAL.—

(A) DETERMINATION.—The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) of this section or section 351(k) of the Public Health Service Act because of any request to take any form of action relating to the application, either before or during consideration of the request, unless—

(i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and

(ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

Consideration of the petition shall be separate and apart from review and approval of any application.

(B) NOTIFICATION.—If the Secretary determines under subparagraph (A) that a delay is necessary with respect to an application, the Secretary shall provide to the applicant, not later than 30 days after making such determination, the following information:

(i) Notification of the fact that a determination under subparagraph (A) has been made.

(ii) If applicable, any clarification or additional data that the applicant should submit to the docket on the petition to allow the Secretary to review the petition promptly.

(iii) A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.

(C) FORMAT.—The information described in subparagraph (B) shall be conveyed via either, at the discretion of the Secretary—

(i) a document; or

(ii) a meeting with the applicant involved.

(D) PUBLIC DISCLOSURE.—Any information conveyed by the Secretary under subparagraph (C) shall be considered part of the application and shall be subject to the disclosure requirements applicable to information in such application.

(E) DENIAL BASED ON INTENT TO DELAY.—If the Secretary determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination. The Secretary may issue guidance to describe the factors that will be used to determine under this subparagraph whether a petition is submitted with the primary purpose of delaying the approval of an application.

(F) FINAL AGENCY ACTION.—The Secretary shall take final agency action on a petition not later than 150 days after the date on which the petition is submitted. The Secretary shall not extend such period for any reason, including—

(i) any determination made under subparagraph (A);

(ii) the submission of comments relating to the petition or supplemental information supplied by the petitioner; or

(iii) the consent of the petitioner.

(G) EXTENSION OF 30-MONTH PERIOD.—If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

(H) CERTIFICATION.—The Secretary shall not consider a petition for review unless the party submitting such petition does so in written form and the subject document is signed and contains the following certification: "I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.", with the date on which such information first became known to such party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(I) VERIFICATION.—The Secretary shall not accept for review any supplemental information or comments on a petition unless the party submitting such information or comments does so in written form and the subject document is signed and contains the following verification: "I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about _____. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.", with the date on which such information first became known to the party and the names of such persons or organizations inserted in the first and second blank space, respectively.

(2) EXHAUSTION OF ADMINISTRATIVE REMEDIES.—

(A) FINAL AGENCY ACTION WITHIN 150 DAYS.—The Secretary shall be considered to have taken final agency action on a petition if—

(i) during the 150-day period referred to in paragraph (1)(F), the Secretary makes a final decision within the meaning of section 10.45(d) of title 21, Code of Federal Regulations (or any successor regulation); or

(ii) such period expires without the Secretary having made such a final decision.

(B) DISMISSAL OF CERTAIN CIVIL ACTIONS.—If a civil action is filed against the Secretary with respect to any issue raised in the petition before the Secretary has taken final agency action on the petition within the meaning of subparagraph (A), the court shall dismiss without prejudice the action for failure to exhaust administrative remedies.

(C) ADMINISTRATIVE RECORD.—For purposes of judicial review related to the approval of an application for which a petition under paragraph (1) was submitted, the administrative record regarding any issue raised by the petition shall include—

(i) the petition filed under paragraph (1) and any supplements and comments thereto;

(ii) the Secretary's response to such petition, if issued; and

(iii) other information, as designated by the Secretary, related to the Secretary's determinations regarding the issues raised in such petition, as long as the information was considered by the agency no later than the date of final agency action as defined under subparagraph (2)(A), and regardless of whether the Secretary responded to the petition at or before the approval of the application at issue in the petition.

(3) ANNUAL REPORT ON DELAYS IN APPROVALS PER PETITIONS.—The Secretary shall annually submit to the Congress a report that specifies—

(A) the number of applications that were approved during the preceding 12-month period;

(B) the number of such applications whose effective dates were delayed by petitions referred to in paragraph (1) during such period;

(C) the number of days by which such applications were so delayed; and

(D) the number of such petitions that were submitted during such period.

(4) EXCEPTIONS.—

(A) This subsection does not apply to—

(i) a petition that relates solely to the timing of the approval of an application pursuant to subsection (j)(5)(B)(iv); or

(ii) a petition that is made by the sponsor of an application and that seeks only to have the Secretary take or refrain from taking any form of action with respect to that application.

(B) Paragraph (2) does not apply to a petition addressing issues concerning an application submitted pursuant to section 351(k) of the Public Health Service Act.

(5) DEFINITIONS.—

(A) APPLICATION.—For purposes of this subsection, the term "application" means an application submitted under subsection (b)(2) or (j) of this section or section 351(k) of the Public Health Service Act.

(B) PETITION.—For purposes of this subsection, other than paragraph (1)(A)(i), the term "petition" means a request described in paragraph (1)(A)(i).

(r) POSTMARKET DRUG SAFETY INFORMATION FOR PATIENTS AND PROVIDERS.—

(1) ESTABLISHMENT.—Not later than 1 year after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, the Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that—

(A) provides links to drug safety information listed in paragraph (2) for prescription drugs that are approved under this section or licensed under section 351 of the Public Health Service Act; and

(B) improves communication of drug safety information to patients and providers.

(2) INTERNET WEB SITE.—The Secretary shall carry out paragraph (1) by—

(A) developing and maintaining an accessible, consolidated Internet Web site with easily searchable drug safety information, including the information found on United States Government Internet Web sites, such as the United States National Library of Medicine's Daily Med and Medline Plus Web sites, in addition to other such Web sites maintained by the Secretary;

(B) ensuring that the information provided on the Internet Web site is comprehensive and includes, when available and appropriate—

(i) patient labeling and patient packaging inserts;

(ii) a link to a list of each drug, whether approved under this section or licensed under such section 351, for which a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations), is required;

(iii) a link to the registry and results data bank provided for under subsections (i) and (j) of section 402 of the Public Health Service Act;

(iv) the most recent safety information and alerts issued by the Food and Drug Administration for drugs approved by the Secretary under this section, such as product recalls, warning letters, and import alerts;

(v) publicly available information about implemented RiskMAPs and risk evaluation and mitigation strategies under subsection (o);

(vi) guidance documents and regulations related to drug safety; and

(vii) other material determined appropriate by the Secretary;

(C) providing access to summaries of the assessed and aggregated data collected from the active surveillance infrastructure under subsection (k)(3) to provide information of known and serious side-effects for drugs approved under this section or licensed under such section 351;

(D) preparing and making publicly available on the Internet website established under paragraph (1) best practices for drug safety surveillance activities for drugs approved under this section or section 351 of the Public Health Service Act;

(E) enabling patients, providers, and drug sponsors to submit adverse event reports through the Internet Web site;

(F) providing educational materials for patients and providers about the appropriate means of disposing of expired, damaged, or unusable medications; and

(G) supporting initiatives that the Secretary determines to be useful to fulfill the purposes of the Internet Web site.

(3) POSTING OF DRUG LABELING.—The Secretary shall post on the Internet Web site established under paragraph (1) the approved professional labeling and any required patient labeling of a drug approved under this section or licensed under such section 351 not later than 21 days after the date the drug is approved or licensed, including in a supplemental application with respect to a labeling change.

(4) PRIVATE SECTOR RESOURCES.—To ensure development of the Internet Web site by the date described in paragraph (1), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

(5) AUTHORITY FOR CONTRACTS.—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subsection.

(6) REVIEW.—The Advisory Committee on Risk Communication under section 567 shall, on a regular basis, perform a comprehensive review and evaluation of the types of risk communication information provided on the Internet Web site established under paragraph (1) and, through other means, shall identify, clarify, and define the purposes and types of information available to facilitate the efficient flow of information to patients and providers, and shall recommend ways for the Food and Drug Administration to work with outside entities to help facilitate the dispensing of risk communication information to patients and providers.

(s) REFERRAL TO ADVISORY COMMITTEE.—Prior to the approval of a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 351 of the Public Health Service Act, the Secretary shall—

(1) refer such drug to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee; or

(2) if the Secretary does not refer such a drug to a Food and Drug Administration advisory committee prior to the approval

of the drug, provide in the action letter on the application for the drug a summary of the reasons why the Secretary did not refer the drug to an advisory committee prior to approval.

(t) DATABASE FOR AUTHORIZED GENERIC DRUGS.—

(1) IN GENERAL.—

(A) PUBLICATION.—The Commissioner shall—

(i) not later than 9 months after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, publish a complete list on the Internet Web site of the Food and Drug Administration of all authorized generic drugs (including drug trade name, brand company manufacturer, and the date the authorized generic drug entered the market); and

(ii) update the list quarterly to include each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug during the preceding 3-month period.

(B) NOTIFICATION.—The Commissioner shall notify relevant Federal agencies, including the Centers for Medicare & Medicaid Services and the Federal Trade Commission, when the Commissioner first publishes the information described in subparagraph (A) that the information has been published and that the information will be updated quarterly.

(2) INCLUSION.—The Commissioner shall include in the list described in paragraph (1) each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug after January 1, 1999.

(3) AUTHORIZED GENERIC DRUG.—In this section, the term "authorized generic drug" means a listed drug (as that term is used in subsection (j)) that—

(A) has been approved under subsection (c); and

(B) is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.

(u) CERTAIN DRUGS CONTAINING SINGLE ENANTIOMERS.—

(1) IN GENERAL.—For purposes of subsections (c)(3)(E)(ii) and (j)(5)(F)(ii), if an application is submitted under subsection (b) for a non-racemic drug containing as an active ingredient (including any ester or salt of the active ingredient) a single enantiomer that is contained in a racemic drug approved in another application under subsection (b), the applicant may, in the application for such non-racemic drug, elect to have the single enantiomer not be considered the same active ingredient as that contained in the approved racemic drug, if—

(A)(i) the single enantiomer has not been previously approved except in the approved racemic drug; and

(ii) the application submitted under subsection (b) for such non-racemic drug—

(I) includes full reports of new clinical investigations (other than bioavailability studies)—

(aa) necessary for the approval of the application under subsections (c) and (d); and

(bb) conducted or sponsored by the applicant; and

(II) does not rely on any clinical investigations that are part of an application submitted under subsection (b) for approval of the approved racemic drug; and

(B) the application submitted under subsection (b) for such non-racemic drug is not submitted for approval of a condition of use—

(i) in a therapeutic category in which the approved racemic drug has been approved; or

(ii) for which any other enantiomer of the racemic drug has been approved.

(2) LIMITATION.—

(A) NO APPROVAL IN CERTAIN THERAPEUTIC CATEGORIES.—Until the date that is 10 years after the date of approval of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph, the Secretary shall not approve such non-racemic drug for any condition of use in the therapeutic category in which the racemic drug has been approved.

(B) LABELING.—If applicable, the labeling of a non-racemic drug described in paragraph (1) and with respect to which the applicant has made the election provided for by such paragraph shall include a statement that the non-racemic drug is not approved, and has not been shown to be safe and effective, for any condition of use of the racemic drug.

(3) DEFINITION.—

(A) IN GENERAL.—For purposes of this subsection, the term "therapeutic category" means a therapeutic category identified in the list developed by the United States Pharmacopeia pursuant to section 1860D–4(b)(3)(C)(ii) of the Social Security Act and as in effect on the date of the enactment of this subsection.

(B) PUBLICATION BY SECRETARY.—The Secretary shall publish the list described in subparagraph (A) and may amend such list by regulation.

(4) AVAILABILITY.—The election referred to in paragraph (1) may be made only in an application that is submitted to the Secretary after the date of the enactment of this subsection and before October 1, 2022.

(v) ANTIBIOTIC DRUGS SUBMITTED BEFORE NOVEMBER 21, 1997.—

(1) ANTIBIOTIC DRUGS APPROVED BEFORE NOVEMBER 21, 1997.—

(A) IN GENERAL.—Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) shall be eligible for, with respect to the drug, the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv)

of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable.

(B) APPLICATION; ANTIBIOTIC DRUG DESCRIBED.—

(i) APPLICATION.—An application described in this clause is an application for marketing submitted under this section after the date of the enactment of this subsection in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) ANTIBIOTIC DRUG.—An antibiotic drug described in this clause is an antibiotic drug that was the subject of an application approved by the Secretary under section 507 of this Act (as in effect before November 21, 1997).

(2) ANTIBIOTIC DRUGS SUBMITTED BEFORE NOVEMBER 21, 1997, BUT NOT APPROVED.—

(A) IN GENERAL.—Notwithstanding any provision of the Food and Drug Administration Modernization Act of 1997 or any other provision of law, a sponsor of a drug that is the subject of an application described in subparagraph (B)(i) may elect to be eligible for, with respect to the drug—

(i)(I) the 3-year exclusivity period referred to under clauses (iii) and (iv) of subsection (c)(3)(E) and under clauses (iii) and (iv) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; and

(II) the 5-year exclusivity period referred to under clause (ii) of subsection (c)(3)(E) and under clause (ii) of subsection (j)(5)(F), subject to the requirements of such clauses, as applicable; or

(ii) a patent term extension under section 156 of title 35, United States Code, subject to the requirements of such section.

(B) APPLICATION; ANTIBIOTIC DRUG DESCRIBED.—

(i) APPLICATION.—An application described in this clause is an application for marketing submitted under this section after the date of the enactment of this subsection in which the drug that is the subject of the application contains an antibiotic drug described in clause (ii).

(ii) ANTIBIOTIC DRUG.—An antibiotic drug described in this clause is an antibiotic drug that was the subject of 1 or more applications received by the Secretary under section 507 of this Act (as in effect before November 21, 1997), none of which was approved by the Secretary under such section.

(3) LIMITATIONS.—

(A) EXCLUSIVITIES AND EXTENSIONS.—Paragraphs (1)(A) and (2)(A) shall not be construed to entitle a drug that is the subject of an approved application described in subparagraphs (1)(B)(i) or (2)(B)(i), as applicable, to any market exclusivities or patent extensions other than those exclusivities or extensions described in paragraph (1)(A) or (2)(A).

(B) CONDITIONS OF USE.—Paragraphs (1)(A) and (2)(A)(i) shall not apply to any condition of use for which the drug referred to in subparagraph (1)(B)(i) or (2)(B)(i), as applicable, was approved before the date of the enactment of this subsection.

(4) APPLICATION OF CERTAIN PROVISIONS.—Notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law, and subject to the limitations in paragraphs (1), (2), and (3), the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to any drug subject to paragraph (1) or any drug with respect to which an election is made under paragraph (2)(A).

(w) DEADLINE FOR DETERMINATION ON CERTAIN PETITIONS.—The Secretary shall issue a final, substantive determination on a petition submitted pursuant to subsection (b) of section 314.161 of title 21, Code of Federal Regulations (or any successor regulations), no later than 270 days after the date the petition is submitted.

(x) DATE OF APPROVAL IN THE CASE OF RECOMMENDED CONTROLS UNDER THE CSA.—

(1) IN GENERAL.—In the case of an application under subsection (b) with respect to a drug for which the Secretary provides notice to the sponsor that the Secretary intends to issue a scientific and medical evaluation and recommend controls under the Controlled Substances Act, approval of such application shall not take effect until the interim final rule controlling the drug is issued in accordance with section 201(j) of the Controlled Substances Act.

(2) DATE OF APPROVAL.—For purposes of this section, with respect to an application described in paragraph (1), the term "date of approval" shall mean the later of—

(A) the date an application under subsection (b) is approved under subsection (c); or

(B) the date of issuance of the interim final rule controlling the drug.

(y) CONTRAST AGENTS INTENDED FOR USE WITH APPLICABLE MEDICAL IMAGING DEVICES.—

(1) IN GENERAL.—The sponsor of a contrast agent for which an application has been approved under this section may submit a supplement to the application seeking approval for a new use following the authorization of a premarket submission for an applicable medical imaging device for that use with the contrast agent pursuant to section 520(p)(1).

(2) REVIEW OF SUPPLEMENT.—In reviewing a supplement submitted under this subsection, the agency center charged with the premarket review of drugs may—

(A) consult with the center charged with the premarket review of devices; and

(B) review information and data submitted to the Secretary by the sponsor of an applicable medical imaging device pursuant to section 515, 510(k), or 513(f)(2) so long as the sponsor of such applicable medical imaging device has provided to the sponsor of the contrast agent a right of reference.

(3) DEFINITIONS.—For purposes of this subsection—

(A) the term "new use" means a use of a contrast agent that is described in the approved labeling of an applicable medical imaging device described in section 520(p), but that is not described in the approved labeling of the contrast agent; and

(B) the terms "applicable medical imaging device" and "contrast agent" have the meanings given such terms in section 520(p).

* * * * * * *

○

Public Law 116–290
116th Congress

An Act

To amend the Federal Food, Drug, and Cosmetic Act regarding the list under section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act, and for other purposes.

Jan. 5, 2021
[H.R. 1503]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

Orange Book Transparency Act of 2020.
21 USC 301 note.

SECTION 1. SHORT TITLE.

This Act may be cited as the "Orange Book Transparency Act of 2020".

SEC. 2. ORANGE BOOK MODERNIZATION.

(a) SUBMISSION OF PATENT INFORMATION FOR BRAND NAME DRUGS.—

(1) IN GENERAL.—Paragraph (1) of section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) is amended to read as follows:

"(b)(1)(A) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as part of the application—

"(i) full reports of investigations which have been made to show whether such drug is safe for use and whether such drug is effective in use; Reports.

"(ii) a full list of the articles used as components of such drug; List.

"(iii) a full statement of the composition of such drug;

"(iv) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

"(v) such samples of such drug and of the articles used as components thereof as the Secretary may require;

"(vi) specimens of the labeling proposed to be used for such drug;

"(vii) any assessments required under section 505B; and Assessments.

"(viii) the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that—

"(I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or

"(II) claims a method of using such drug for which approval is sought or has been granted in the application.

"(B) If an application is filed under this subsection for a drug, and a patent of the type described in subparagraph (A)(viii) is issued after the filing date but before approval of the application, the applicant shall amend the application to include the patent number and expiration date.".

(b) SUBSEQUENT SUBMISSION OF PATENT INFORMATION.—

Deadlines.

(1) IN GENERAL.—Section 505(c)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(c)(2)) is amended—

(A) by inserting before the first sentence the following: "Not later than 30 days after the date of approval of an application submitted under subsection (b), the holder of the approved application shall file with the Secretary the patent number and the expiration date of any patent described in subsection (b)(1)(A)(viii), except that a patent that is identified as claiming a method of using such drug shall be filed only if the patent claims a method of use approved in the application. If a patent described in subsection (b)(1)(A)(viii) is issued after the date of approval of an application submitted under subsection (b), the holder of the approved application shall, not later than 30 days after the date of issuance of the patent, file the patent number and the expiration date of the patent, except that a patent that claims a method of using such drug shall be filed only if approval for such use has been granted in the application.";

(B) in the first sentence following the sentences added by subparagraph (A), by striking "which claims the drug for which" and all that follows through "of the drug." and inserting "described in subsection (b)(1)(A)(viii).";

(C) in the second sentence following the sentences added by subparagraph (A), by inserting after "could not file patent information under subsection (b) because no patent" the following: "of the type for which information is required to be submitted in subsection (b)(1)(A)(viii)"; and

(D) by adding at the end the following: "Patent information that is not the type of patent information required by subsection (b)(1)(A)(viii) shall not be submitted under this paragraph.".

(2) UPDATING LIST.—Clause (iii) of section 505(j)(7)(A) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) is amended by striking "(b) or".

(c) LISTING OF EXCLUSIVITIES.—Subparagraph (A) of section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) is amended by adding at the end the following:

"(iv) For each drug included on the list, the Secretary shall specify any exclusivity period that is applicable, for which the Secretary has determined the expiration date, and for which such period has not yet expired, under—

"(I) clause (ii), (iii), or (iv) of subsection (c)(3)(E);
"(II) clause (iv) or (v) of paragraph (5)(B);
"(III) clause (ii), (iii), or (iv) of paragraph (5)(F);
"(IV) section 505A;
"(V) section 505E;
"(VI) section 527(a); or
"(VII) subsection (u).".

(d) ORANGE BOOK UPDATES WITH RESPECT TO INVALIDATED PATENTS.—

(1) AMENDMENT.—Section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)) is amended by adding at the end the following:

"(D) In the case of a listed drug for which the list under subparagraph (A)(i) includes a patent for such drug, and any claim of the patent has been cancelled or invalidated pursuant to a final decision issued by the Patent Trial and Appeal Board of the United States Patent and Trademark Office or by a court, from which no appeal has been, or can be, taken, if the holder of the applicable application approved under subsection (c) determines that a patent for such drug, or any patent information for such drug, no longer meets the listing requirements under this section— Determination.

"(i) the holder of such approved application shall notify the Secretary, in writing, within 14 days of such decision of such cancellation or invalidation and request that such patent or patent information, as applicable, be amended or withdrawn in accordance with the decision issued by the Patent Trial and Appeal Board or a court; Notification. Deadline.

"(ii) the holder of such approved application shall include in any notification under clause (i) information related to such patent cancellation or invalidation decision and submit such information, including a copy of such decision, to the Secretary; and

"(iii) the Secretary shall, in response to a notification under clause (i), amend or remove patent or patent information in accordance with the relevant decision from the Patent Trial and Appeals Board or court, as applicable, except that the Secretary shall not remove from the list any patent or patent information before the expiration of any 180-day exclusivity period under paragraph (5)(B)(iv) that relies on a certification described in paragraph (2)(A)(vii)(IV).".

(2) APPLICABILITY.—Subparagraph (D) of section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), as added by paragraph (1), applies only with respect to a decision described in such subparagraph that is issued on or after the date of enactment of this Act. 21 USC 355 note.

(e) REVIEW AND REPORT.—Not later than 1 year after the date of enactment of this Act, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs, shall—

(1) solicit public comment regarding the types of patent information that should be included on, or removed from, the list under section 507(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)); and

(2) transmit to Congress a summary of such comments and actions the Food and Drug Administration is considering taking, if any, in response to public comment pursuant to paragraph (1) about the types of patent information that should be included or removed from such list. Summary.

(f) GAO REPORT TO CONGRESS.—

(1) IN GENERAL.—Not later than 2 years after the date of enactment of this Act, the Comptroller General of the United States (referred to in this section as the "Comptroller General") shall submit to the Committee on Health, Education, Labor, Analysis.

and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report on the patents included in the list published under section 505(j)(7) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355(j)(7)) that claim an active ingredient or formulation of a drug in combination with a device that is used for delivery of such drug, including an analysis of such patents and their claims.

(2) CONTENT.—The Comptroller General shall include in the report under paragraph (1)—

Data.

(A) data on—

(i) the number of patents included in the list published under section 505(j)(7) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355(j)(7)) that claim the active ingredient or formulation of a drug in combination with a device that is used for delivery of the drug, and that together claim the finished dosage form of the drug; and

(ii) the number of claims with respect to each patent included in the list published under such section 505(j)(7) that claim a device that is used for the delivery of the drug, but do not claim such device in combination with an active ingredient or formulation of a drug;

Analysis.

(B) an analysis of the listing of patents described in subparagraph (A)(ii), including the timing of listing such patents in relation to patents described in subparagraph (A)(i), and the effect listing the patents described in subparagraph (A)(ii) has on market entry of one or more drugs approved under section 505(j) of the Federal Food, Drug, and Cosmetic Act as compared to the effect of not listing the patents described in subparagraph (A)(ii); and

Recommendations.

(C) recommendations about which kinds of patents relating to devices described in subparagraph (A)(i) should be submitted to the Secretary of Health and Human Services for inclusion on the list under section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act and which patents should not be required to be so submitted in order to reduce barriers to approval and market entry.

(g) CONFORMING AMENDMENTS.—Section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) is amended—

(1) in subsection (c)(3)(E), by striking "clause (A) of subsection (b)(1)" each place it appears and inserting "subsection (b)(1)(A)(i)"; and

(2) in subsection (j)(2)(A)(vi), by striking "clauses (B) through (F) of subsection (b)(1)" and inserting "clauses (ii) through (vi) of subsection (b)(1)(A)".

Approved January 5, 2021.

LEGISLATIVE HISTORY—H.R. 1503:

HOUSE REPORTS: No. 116–47 (Comm. on Energy and Commerce).
CONGRESSIONAL RECORD:
Vol. 165 (2019): May 8, considered and passed House.
Vol. 166 (2020): Dec. 7, considered and passed Senate, amended.
Dec. 10, House concurred in Senate amendment.

○

results or that are inconsistent with common sense." *Bonkowski v. Oberg Indus., Inc.*, 787 F.3d 190, 200 (3d Cir. 2015) (quotation omitted).

Critically, as a matter of law, under the FDCA, FDA cannot classify a "device" as a "drug." *Genus Medical Techs. LLC v. FDA*, 994 F.3d 631, 632-33 (D.C. Cir. 2021). As detailed in *Genus Medical*, the FDCA defines both "drug" and "device."[3] Although the two definitions overlap, the "device" definition excludes products that work primarily through "chemical action within or on the body of man" or through "metabolization." *Genus Medical*, 994 F.3d at 637-38; 21 U.S.C. § 321(h)(1).

In *Genus Medical*, the D.C. Circuit considered the "purely legal" question of whether in view of these definitions, "the FDCA grants [the FDA] discretion to classify as a 'drug' any product that meets the statutory definition of a 'device'." *Id*. at 632, 644. After analyzing the definitions and considering "the text, statutory structure and legislative history" of the FDCA, the court held that the FDCA prohibits FDA from classifying something as a "drug" if it meets the definition of a

[3] *Id*. at 633; *see* 21 U.S.C. §§ 321(g)(1), (h)(1). The definition of "device" in § 321(h)(1) specifies that it does not apply in certain sections of Title 21, but that list of exclusions does not include § 355. The definition of "drug" in § 321(g) does not exclude any sections from its applicability. Thus, both definitions apply to § 355, which contains the Listing Criteria.

presence of a drug substance, then a drug product *patent* must also require the presence of a drug substance.[7]

Moreover, the legislative history of the Orange Book Transparency Act of 2020 ("OBTA") confirms that the Drug Substance and Drug Product criteria exclude device patents and should be narrowly construed. The only substantive change the OBTA made to the Listing Criteria was to add the Drug Substance and Drug Product criteria; the other criteria were merely reworded. *Compare* Conroy Ex. 8, H.R. Rep. No. 116-47 at 9-10 (2019) (reciting then-existing law in brackets, which included that "[t]he applicant shall file . . . any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug . . . .") *with* Conroy Ex. 9, Orange Book Transparency Act of 2020, Pub. L. No. 116-

[7] Teva argues that because the FDA regulation prohibits submitting certain kinds of patents (process, packaging, metabolites, and intermediates) for listing, "other types of patents" are listable. (D.I. 27 at 17.) Teva is wrong, at least with respect to device patents. Nothing in the regulation suggests that the list of excluded patents is exhaustive. Also, Teva's argument improperly relies on the inclusion/exclusion principle of statutory interpretation, even though 21 C.F.R. § 314.53 is a *regulation*, not a statute. Finally, even if applicable to a regulation, the principle is not implicated here, because the FDA did not *include* device patents elsewhere in the regulations, only to *exclude* them from the recitation of un-listable patent types.

290, 134 Stat. 4889 at Section (b)(1)(A)(viii) (Jan. 5, 2021) (adding clause (I) with the Drug Substance and Drug Product criteria).

As the Committee Report[8] for the OBTA demonstrates, the Drug Substance and Drug Product criteria were introduced expressly to preclude Orange Book listing of the very type of device patents that Teva improperly listed for ProAir® HFA. Committee reports are a particularly authoritative source for interpreting a statute. *Garcia v. U.S.*, 469 U.S. 70, 76 (1984). Here, when the Committee Report set forth the "Background and Need for Legislation," it explained that:

> While FDA has issued regulations clarifying certain types of patents that must be submitted . . . and certain types that must not be submitted, many patents are complex and may not fall clearly into the types identified by FDA. As a result, **some branded drug manufacturers . . . are submitting patents potentially for the purpose of blocking generic competition.**[3] . . . This legislation would help to ensure that the Orange Book is accurate and up-to-date, by specifying what information must be submitted to FDA and what information should be listed . . . .

Conroy Ex. 8, H.R. Rep. No. 116-47 at 4 (2019) (emphasis added) (footnote in original).

---

[8] This report was prepared by the Committee on Energy and Commerce. Congressional committee reports accompany legislative measures when they are reported for chamber action and explain the proposed legislation and its intended effects in detail. These reports also offer the assigned committee's findings and recommendations.

To support the observation that some branded drug manufacturers may be submitting patents "for the purpose of blocking competition," in footnote 3, the Committee Report cited a 2018 article published in *Nature Biotechnology*. *Id*. That article analyzed the proliferation of device patents in the Orange Book for drug-device combination products, including, most commonly, *inhalers*. (*See* Conroy Ex. 3 at 142-43 (reporting that "[t]he most common such products were inhalers . . ." and that "market exclusivity extensions" from drug delivery device patents listed with the FDA were "particularly common among pens and inhalers.").) The supporting data for this article expressly included the Orange Book listing for ProAir® HFA.[9]

Further, amendments made to the OBTA before it was passed into law show that the Drug Substance and Drug Product criteria should be narrowly construed.

---

[9] Supporting Data to Ex. 3 at row 7 (available at https://static-content.springer.com/esm/art%3A10.1038%2Fnbt.4078/MediaObjects/41587_2018_BFnbt4078_MOESM2_ESM.xlsx) (last accessed Feb 20, 2024) (listing ProAir® HFA by name). The Court may consider the substance of this article and its supplemental information without converting Amneal's motion to a motion for summary judgment. The article is a public document and is referred to in the legislative history. It is not offered for the truth of the statements it contains, but rather for the fact that it contains those statements. It therefore can be considered for the purposes of statutory interpretation, a legal question, and the Court may take judicial notice of it without converting to summary judgment. *See* Fed. R. Evid. 201; *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 322 (2007); *Oran v. Stafford*, 226 F.3d 275, 289 (3d Cir. 2000).

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., AND TEVA PHARMACEUTICALS USA, INC. Plaintiffs, v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS LLC, AND AMNEAL PHARMACEUTICALS INC. Defendants.	Civil Action No. 2:23-cv-20964-JXN-MAH

PLEASE TAKE NOTICE that the Federal Trade Commission will move before Magistrate Judge Michael A. Hammer, on April 1, 2024, for an Order granting the Commission leave to file the attached amicus brief pursuant to the Court's minute entry at ECF No. 51. No party opposes this motion.

PLEASE TAKE FURTHER NOTICE that in support of the unopposed motion, the Federal Trade Commission will rely on the attached memorandum of law. A proposed order has also been submitted with this motion.

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., AND TEVA PHARMACEUTICALS USA, INC. Plaintiffs, v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS LLC, AND AMNEAL PHARMACEUTICALS INC. Defendants.	Civil Action No. 2:23-cv-20964-JXN-MAH

MEMORANDUM IN SUPPORT OF THE FEDERAL TRADE COMMISSION'S UNOPPOSED MOTION FOR LEAVE TO FILE AS AMICUS CURIAE

The pending dispositive motions in this case raise significant competition issues with market-wide implications extending beyond the parties' private dispute. The Federal Trade Commission (FTC), as an independent agency charged with protecting competition, represents the public interest and brings important expertise to these proceedings.

By filing this patent infringement case under the Hatch Waxman Act, Teva has delayed FDA approval of Amneal's proposed inhaler product by up to 30 months. Amneal counterclaims that the patents at issue were not properly listed in the FDA's Orange Book. The FTC has long maintained that impeding entry of competitors through improperly listed patents can violate competition laws. Further, FTC staff recently addressed the specific patents at issue here, publicly calling for Teva to remove them from Orange Book.

The attached amicus brief addresses issues not fully explored in the party briefs, including (1) the extent to which device and device component patents may be properly listed in the Orange Book, including but not limited to the patents at issue in this case; (2) the harms that may result from improperly listing patents, particularly with regard to inhaler products; (3) the availability of standalone antitrust claims based on improper patent listings; and (4) the strong public interest against immunizing improper Orange Book listings from antitrust liability.

Thus, the FTC respectfully requests leave to file the attached amicus brief.

I. Courts Have Broad Discretion to Appoint Amicus Curiae and Look Favorably on Government Agencies Seeking Such Appointment

"District courts have broad discretion to appoint *amicus curiae*."[1] Although there is "no rule governing the appearance of an *amicus curiae* in the United States District Courts," courts in this District look to the Federal Rules of Appellate Procedure for guidance in exercising their broad discretion.[2] Rule 29 of the Federal Rules of Appellate Procedure distinguishes between amicus briefs filed by federal governmental agencies and those filed by private parties. Unlike amicus briefs filed by private parties, those from federal agencies are accepted by Courts of Appeals as a matter of right,[3] and some courts in this district have accepted amicus filings solely on that basis.[4] Favorable treatment of proposed amicus filings by the federal government reflects the understanding that "governmental bodies, acting as amicus curiae, possess unparalleled institutional expertise and constitute a valuable

---

[1] *Liberty Lincoln Mercury, Inc. v. Ford Mktg. Corp.*, 149 F.R.D. 65, 82 (D.N.J. 1993).

[2] *See United States v. Alkaabi*, 223 F. Supp. 2d 583, 592 (D.N.J. 2002) (stating that "the Third Circuit's application of Fed. R. App P. 29… provides guidance to this Court").

[3] Fed. R. App. P. 29(a)(2).

[4] *See, e.g., Clark v. Actavis Group HF*, 567 F. Supp. 2d 711, 718 n.11 (D.N.J. 2008) (accepting amicus brief filed by U.S. Department of Justice, citing Fed. R. App. P. 29).

means of determining how the court's decision may affect the world outside its chambers."[5]

II. The Court Should Exercise its Discretion to Accept an FTC *Amicus* Brief

Courts in this district typically approve amici participation when: "(1) the amicus curiae has a 'special interest' in the particular case; (2) the amicus curiae's interest is not represented competently or at all in the case; (3) the proffered information is timely and useful; and (4) the petitioner is not partial to a particular outcome in the case."[6] The FTC satisfies these criteria..

First, as an independent commission charged with protecting competition, the FTC has a special interest, and a long history of expertise, in the broad competitive implications of abuse of the Hatch Waxman patent listing process, including with regard to improper Orange Book patent listings. Over the last two-plus decades, the FTC has sued over improper patent listings,[7] conducted an

[5] Michael K. Lowman, *The Litigating Amicus Curiae: When Does the Party Begin After the Friends Leave?*, 41 Am. U. L. Rev.1243, 1261–62 (1992).
[6] *Prof'l Drug Co. Inc. v. Wyeth Inc.*, No. 11–5479, 2012 WL 4794587, *1 (D.N.J. 2012) (quoting *Liberty Res., Inc. v. Philadelphia Hous. Auth.*, 395 F. Supp. 2d 206, 209 (E.D. Pa. 2005)).
[7] *See In re Biovail Corp.*, FTC Dkt. No. C-4060 (Oct. 2, 2002).

industry study,[8] and filed multiple amicus briefs relating to the issue.[9] In September 2023, the FTC issued a policy statement concerning improper Orange Book listings and the resulting competitive consequences, explaining that using inappropriately listed patents in the Orange Book to obtain a 30-month stay of competition may have serious long-term implications for all consumers, not just the private parties in this case.[10] In addition, as part of a November 2023 effort to address more than 100 Orange Book improper patent listings by 10 pharmaceutical companies, FTC staff recently disputed Orange Book listings for the specific patents at issue in this case using FDA regulatory procedures available to any person.[11] Concurrently, FTC staff sent these companies, including Teva, letters

---

[8] *See* Fed. Trade Comm'n, Generic Drug Entry Prior to Patent Expiration: An FTC Study, 39-52 (2002), https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patentexpiration-ftc-study/genericdrugstudy_0.pdf.

[9] Mem. of Law of Fed. Trade Comm'n as *Amicus Curiae* Opposing Defendant's Mot. to Dismiss, *In re: Buspirone Patent Litig.*, No. 1:01-md-1410, ECF No. 31 (S.D.N.Y. Jan. 8, 2002); Fed. Trade Comm'n's Brief as Amicus Curiae, *Jazz Pharms. Inc. v. Avadel CNS Pharms., LLC*, C.A. No. 1:21-cv-00691, ECF No. 222-3 (D. Del. Nov. 10, 2022); Fed. Trade Comm'n's Brief as Amicus Curiae, *Mylan Pharms. Inc., et al. v. Sanofi-Aventis U.S. LLC, et al.*, C.A. No. 2:23-cv-00836, ECF No. 61-3 (W.D. Pa. Nov. 20, 2023).

[10] Fed. Trade Comm'n. Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in the Orange Book (Sept. 14, 2023) ("FTC Orange Book Statement") https://www.ftc.gov/system/files/ftc_gov/pdf/p239900orangebookpolicystatement092023.pdf.

[11]. *See* Fed. Trade Comm'n, Press Release, FTC Challenges More Than 100 Patents As Improperly Listed in the FDA's Orange Book (Nov. 7, 2023),

informing them of the regulatory disputes and requesting that they remove the improper patent listings from the Orange Book.[12]

As the primary antitrust enforcer in the pharmaceutical industry, the FTC has a special interest in the interpretation of laws impacting generic drug competition. Courts consider these interests when granting motions for leave to federal agencies to participate as amicus curiae.[13]

Second, the Commission's interests, and the public interest, are not adequately represented by the private parties litigating this case. The parties are each pharmaceutical companies representing their own business interests. The Commission, on the other hand, is a federal agency charged with protecting consumers from practices that create anticompetitive conditions and raise prices. Improper submission of patents for listing in the Orange Book may impair competitive conditions and result in higher costs to consumers.[14]

---

https://www.ftc.gov/news-events/news/press-releases/2023/11/ftc-challenges-more-100-patents-improperly-listed-fdas-orange-book

[12] *Id*.

[13] *See, e.g.*, *Waste Mgmt. of Pa., Inc. v. City of York*, 162 F.R.D. 34, 37 (M.D. Pa. 1995) (stating as a basis for accepting an amicus brief that "the EPA has a special interest in this litigation as it is the primary body responsible for administering and enforcing" the relevant law).

[14] *See* FTC Orange Book Statement, *supra* note 10, at 1; Fed. Trade Comm'ns Br. as Amicus Curiae, *Jazz Pharms. Inc. v. Avadel CNS Pharms., LLC*, C.A. No. 1:21-cv-00691, ECF No. 222-3 (D. Del. Nov. 10, 2022).

Third, the proposed amicus brief provides useful information based on the FTC's extensive knowledge of pharmaceutical competition. The brief outlines the relevant regulatory structure, explains how the regulatory setting may influence antitrust analysis, addresses proper legal standards for listing patents in the Orange Book, and explains that Amneal's antitrust counterclaims are not supplanted by the Hatch Waxman Act.

The FTC's motion for leave is also timely because the Court granted the FTC's consented-to request to file this motion for leave today, March 22, 2024.[15] Teva is not prejudiced by the filing of this brief, particularly since subsequent to the Court's granting the FTC permission to file for leave, Teva received an extension on its next brief until April 15, 2024.[16] Hence, Teva will have more than three weeks to consider and respond to the attached amicus brief. Lack of prejudice is strongly reinforced by Teva's non-opposition to this motion.

Fourth, the FTC does not take a position on the ultimate outcome of the commercial dispute between the parties in this case. Although the FTC takes the position that the Orange Book listings for the asserted patents are improper and such listing may provide a basis for standalone antitrust claims, and has a strong

[15] Order Granting the Fed. Trade Comm'n Permission to File a Mot. Seeking Leave to File an Amicus Br., ECF No. 54.

[16] Letter Order, ECF No. 58 (minute order providing Teva's "consolidated opposition papers to Amneal's motion and reply brief due on 4/15/2024").

interest in the sound development of the law in this area,[17] the FTC takes no position on Teva's patent infringement claims or the amount of damages, if any, that should be awarded to either party on its claims or counterclaims.

III. Conclusion

For the foregoing reasons, the FTC respectfully requests the Court grant it leave to file the attached brief as amicus curiae.

Dated: March 22, 2024

Respectfully submitted,

Hannah Garden-Monheit
Director, Office of Policy Planning

Henry Liu
Director, Bureau of Competition

Anisha Dasgupta
General Counsel, Federal Trade Commission

/s/ Bradley J. Vettraino
Bradley J. Vettraino
Ian Barlow
Rahul Rao
Anupama Sawkar
Matthew Frank
Clarke Edwards
Jordan Klimek
600 Pennsylvania Avenue N.W.
Washington, D.C. 20580
Telephone: (202) 386-2652

[17] Courts "regularly allow[]" amicus filings advocating "policy interests" like the FTC's here. *Alkaabi*, 223 F. Supp. 2d at 592.

CERTIFICATE OF SERVICE

Pursuant to Local Rule 5.2(14)(b)(1), I, Bradley J. Vettraino, an attorney with the Federal Trade Commission, hereby certify that the foregoing document was served on all counsel of record through the Court's CM/ECF system on March 22, 2024.

/s/ Bradley J. Vettraino
Bradley J. Vettraino

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., AND TEVA PHARMACEUTICALS USA, INC. Plaintiffs, v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS LLC, AND AMNEAL PHARMACEUTICALS INC. Defendants.	Civil Action No. 2:23-cv-20964-JXN-MAH

FEDERAL TRADE COMMISSION'S BRIEF AS AMICUS CURIAE

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Other Authorities

Regulations

INTRODUCTION

Listing a patent in the Orange Book gives a brand pharmaceutical company a powerful tool—the ability to trigger a 30-month stay of approval of a generic competitor product. The Federal Trade Commission (FTC or Commission) has a long history of working to address improper Orange Book patent listings because of how those listings thwart competition from lower-cost generic drugs.

Amneal alleges that Teva's improper listing of patents for dose counters and inhaler devices in the Orange Book is delaying entry of its less expensive generic asthma inhalers from summer 2024 to early 2026.[1] Millions of Americans rely on asthma inhalers for life-saving treatment, and the patent on the active ingredient in many asthma inhalers—albuterol—expired in 1989. Although albuterol has long been off-patent, there remains little generic competition in the market for asthma inhalers, in part because brand manufacturers improperly list patents that claim device-related aspects of asthma inhalers, like dose counters, to block competition. As a result, asthma inhalers often cost hundreds of dollars, although they would likely cost significantly less in a more competitive market.

Because improper Orange Book listings can effectively block competition, Congress carefully prescribed what types of patents must be listed in the Orange

[1] *See* Def.'s Answer, Affirmative Defenses, and Countercl. to Pl.s' First Am. Compl., ECF No. 12 ¶¶ 121-22, 130 ("Amneal Countercl."). At this stage in the proceedings, these allegations are accepted as true.

Book, permitting only drug substance, drug product, and method of use patents on Food and Drug Administration (FDA) approved drugs to be listed. Here, however, Teva has triggered a 30-month stay based on inhaler and dose counter device patents that, on their face, are not specific to any FDA-approved drug. Indeed, one of the asserted patents (U.S. Patent No. 10,561,808) has been listed in the Orange Book for 21 different products spanning six separate new drug applications (NDA) and four active ingredients.[2]

In the FTC's view, device patents that do not mention any drug in their claims do not meet the statutory criteria for Orange Book listing, and a device patent that is improperly listed in the Orange Book must be delisted. Should a brand manufacturer not voluntarily delist an improperly listed device patent, it is well within the powers of a district court to compel delisting. Here, Teva has listed device patents in the Orange Book that do not mention any drug in their claims. If the Court agrees that such patents do not meet the listing requirements, it should grant Amneal's motion for judgment on the pleadings and order Teva to delist the patents at issue—clearing the way for Americans to access less expensive asthma inhalers.

[2] *See* U.S. Dep't Health & Hum. Servs., Food & Drug Admin., *Approved Drug Products with Therapeutic Equivalence Evaluations* ADA 7, 39-40, 178-188 (44th ed. 2024) ("Orange Book").

Teva's arguments opposing delisting are unavailing and inconsistent with the statute. Indeed, in a strikingly similar case, the First Circuit rightly held it improper to list a device patent that did not mention the active ingredient or the drug product in the claims. Moreover, Teva's novel argument that the delisting provision immunizes its conduct from the antitrust laws is wrong. Courts and the FTC, the expert body charged with protecting fair competition in pharmaceutical markets, have long recognized that improper Orange Book listings can be actionable under the antitrust laws.

INTEREST OF THE FEDERAL TRADE COMMISSION

The FTC is an independent agency charged by Congress with enforcing competition and consumer protection laws.[3] It exercises primary responsibility for federal antitrust enforcement in the pharmaceutical industry.[4] The Commission has substantial experience evaluating pharmaceutical competition under the Hatch-Waxman Act and has brought numerous enforcement actions challenging anticompetitive abuses of the Hatch-Waxman framework.[5]

---

[3] 15 U.S.C. §§ 41-58.

[4] For a recent summary of the FTC's actions in the pharmaceutical industry, *see* Bradley S. Albert et al., Overview of FTC Actions in Pharm. Products and Distrib., Fed Trade Comm'n (Jan. 2024), https://www.ftc.gov/system/files/ftc_gov/pdf/Overview-Pharma.pdf.

[5] *See, e.g.*, *FTC v. Actavis, Inc.*, 570 U.S. 136 (2013); *King Drug Co. of Florence, Inc. v. Cephalon, Inc.*, 88 F. Supp. 3d 402 (E.D. Pa. 2015); *Impax Labs, Inc. v. FTC*, 994 F.3d 484 (5th Cir. 2021); *FTC v. AbbVie Inc.*, 976 F.3d 327 (3d Cir. 2020); *FTC v. Shkreli*, 581 F. Supp. 3d 579 (S.D.N.Y. 2022).

The FTC has long been concerned about abusive Orange Book listings because of how improper listings may delay and deter competition from less expensive generic drugs. The Commission first examined the effect of Orange Book listings on competition as part of a 2002 study, identifying numerous instances in which companies used the 30-month stay to block competition.[6] Around the same time, the FTC successfully settled an action under the antitrust laws against Biovail Corporation for, among other things, wrongfully listing a patent in the Orange Book to block generic competition.[7]

The FTC has also regularly filed amicus briefs in private litigation, explaining how improper Orange Book listings can violate the antitrust laws.[8] In September 2023, the FTC issued a policy statement, supported by the FDA, warning that improperly listing patents in the Orange Book may constitute illegal

[6] *See* Fed. Trade Comm'n, Generic Drug Entry Prior to Patent Expiration: An FTC Study, 39-52 (2002) ("FTC Study on Generic Drug Entry Before Patent Expiration"), https://www.ftc.gov/reports/generic-drug-entry-prior-patent-expiration-ftc-study.

[7] Decision & Order, *In re Biovail Corp.*, FTC Dkt. No. C-4060 8 (Oct. 2, 2002).

[8] *See* Mem. of Law for Fed. Trade Comm'n as Amicus Curiae, *In re: Buspirone Patent Litig.*, No. 1:01-md-1410, ECF No. 31 (S.D.N.Y. Jan. 8, 2002); Mem. of Law for Fed. Trade Comm'n as Amicus Curiae, *Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC*, No. 1:21-cv-691, ECF No. 227 (D. Del. Nov. 15, 2022); Mem. of Law for Fed. Trade Comm'n as Amici Curiae, *Mylan Pharms. Inc. v. Sanofi-Aventis U.S. LLC*, No. 2:23-cv-00836, ECF No. 64 (W.D. Pa. Nov. 21, 2023).

monopolization under section 2 of the Sherman Act as well as an unfair method of competition under section 5 of the FTC Act.[9]

Last November, the FTC's Bureau of Competition sent warning letters to ten drug manufacturers notifying them of more than 100 Orange Book patent listings that FTC staff believes to be improper ("warning letters").[10] The warning letters identified patents listed on 13 inhaler products and four epinephrine injector pens, among other FDA-approved products. Two of the warning letters were sent to Teva and identified the five patents at issue in this case (the "asserted patents") as

[9] *See* Fed. Trade Comm'n, Federal Trade Commission Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in the Orange Book, at 5-6 (Sept. 14, 2023) ("FTC Orange Book Policy Statement"), https://www.ftc.gov/system/files/ftc_gov/pdf/p239900orangebookpolicystatement092023.pdf; *see also* Fed. Trade Comm'n, Press Release, FTC Issues Policy Statement on Brand Pharmaceutical Manufacturers' Improper Listing of Patents in the Food and Drug Administration's 'Orange Book' (Sep. 14, 2023) ("FTC Press Release re: Orange Book Policy Statement"), https://www.ftc.gov/news-events/news/press-releases/2023/09/ftc-issues-policy-statement-brand-pharmaceutical-manufacturers-improper-listing-patents-food-drug ("The FDA appreciates and supports the FTC's efforts to examine whether brand drug companies are impeding generic drug competition by improperly listing patents in the Orange Book,' said FDA Commissioner Robert M. Califf, M.D.").

[10] *See* Fed. Trade Comm'n, Press Release, FTC Challenges More Than 100 Patents As Improperly Listed in the FDA's Orange Book (Nov. 7, 2023) (FTC Press Release re: Improper Orange Book Listings"), https://www.ftc.gov/news-events/news/press-releases/2023/11/ftc-challenges-more-100-patents-improperly-listed-fdas-orange-book.The patents identified in the warning letters should not be interpreted as an exclusive or exhaustive list of patents that the FTC believes are wrongfully listed, and companies that did not receive a letter in November 2023 should not assume the FTC views their listings as proper. The FTC continues to scrutinize whether additional patents are improperly listed, and all companies have an ongoing responsibility to ensure their listings are lawful.

well as 37 additional Teva patent listings on inhalers.[11] The letters notified Teva and other drug companies that the FTC was utilizing FDA's regulatory patent listing dispute process to challenge the improper listings, while retaining the right to take further action against the companies that the public interest may require, including investigating the conduct as an unfair method of competition under section 5 of the FTC Act.

In response to the warning letters, several companies, including GlaxoSmithKline, Kaleo, Inc., and Impax Laboratories LLC, delisted 14 patents across six NDAs. Meanwhile, AstraZeneca, Boehringer Ingelheim, and GlaxoSmithKline announced that they would reduce patient out-of-pocket costs for all of their asthma inhalers to $35 a month.[12] Following the warning letters,

---

[11] *See* Letter from Rahul Rao, Dep. Dir., Bur. Competition, Fed. Trade Comm'n to Teva Branded Pharm. Prods. R&D, Inc. Regarding Improper Orange Book-Listed Patents for QVAR 40, ProAir HFA, ProAir DigiHaler (Nov. 7, 2023) ("Teva Warning Letter"), https://www.ftc.gov/system/files/ftc_gov/pdf/teva-branded-pharma-orange-book.pdf (disputing propriety of 35 patent listings, comprised of 18 patents across 3 inhaler products); Letter from Rahul Rao, Dep. Dir., Bur. Competition, Fed. Trade Comm'n to Norton (Waterford) Ltd. Regarding Improper Orange Book-Listed Patents for QVAR RediHaler (Nov. 7, 2023) ("Norton Warning Letter"), https://www.ftc.gov/system/files/ftc_gov/pdf/norton-orange-book.pdf (disputing propriety of 7 patent listings on 1 inhaler product).

[12] *See* Press Release, AstraZeneca, AstraZeneca caps patient out-of-pocket costs at $35 per month for its US inhaled respiratory portfolio (Mar. 18, 2024), https://www.astrazeneca-us.com/media/press-releases/2024/astrazeneca-caps-patient-out-of-pocket-costs-at-35-per-month-for-its-us-inhaled-respiratory-portfolio.html; Press Release, Boehringer Ingelheim, Boehringer Ingelheim caps patient out-of-pocket costs for its inhaler portfolio at $35 per month (Mar. 7,

numerous members of Congress also launched inquiries into the drug companies' Orange Book listings and other potentially anticompetitive practices.[13]

The warning letters to Teva explained FTC staff's belief that the patents at issue in this case—plus many others—are improperly listed in the Orange Book.

2024), https://www.boehringer-ingelheim.com/us/press-releases/boehringer-ingelheim-caps-patient-out-of-pocket-costs-inhaler-portfolio; Press Release, GlaxoSmithKline, GSK announces cap of $35 per month on U.S. patient out-of-pocket costs for its entire portfolio of asthma and COPD inhalers (Mar. 20, 2024), https://us.gsk.com/en-us/media/press-releases/gsk-announces-cap-of-35-per-month-on-us-patient-out-of-pocket-costs-for-its-entire-portfolio-of-asthma-and-copd-inhalers. While the Commission welcomes voluntarily reductions in patients' out-of-pocket costs, doing so is not a substitute for removing improper patent listings, as such listings may delay competition from generics with lower list prices.

[13] *See* Press Release, U.S. Sen. Comm. On Health, Educ. Labor and Pensions, Chairman Sanders, Baldwin, Luján, Markey Launch HELP Committee Investigation into Efforts by Pharmaceutical Companies to Manipulate the Price of Asthma Inhalers (Jan. 8, 2024), https://www.help.senate.gov/chair/newsroom/press/news-chairman-sanders-baldwin-lujan-markey-launch-help-committee-investigation-into-efforts-by-pharmaceutical-companies-to-manipulate-the-price-of-asthma-inhalers; Letter from Sen. Bernie Sanders et al. to Pascal Soriot, Exec. Dir. & Chief Exec. Off., AstraZeneca PLC (Jan. 8, 2024), https://www.sanders.senate.gov/wp-content/uploads/2024.01.08-HELP-Committee-Letter-to-AstraZeneca.pdf; Letter from Sen. Bernie Sanders et al. to Hubertus von Baumbach, Chairman of the Bd. Of Managing Dirs., Boehringer Ingelheim Int'l GmbH (Jan. 8, 2024), https://www.sanders.senate.gov/wp-content/uploads/2024.01.08-HELP-Committee-Letter-to-Boehringer-Ingelheim.pdf; Letter from Sen. Bernie Sanders et al. to Emma Walmsley, Chief Exec. Off., GSK (Jan. 8, 2024), https://www.sanders.senate.gov/wp-content/uploads/2024.01.08-HELP-Committee-Letter-to-Boehringer-Ingelheim.pdf; Letter from Sen. Bernie Sanders et al. to Richard Francis, Pres. & Chief Exec. Off., Teva Pharm. Indus. Ltd. (Jan. 8, 2024), https://www.sanders.senate.gov/wp-content/uploads/2024.01.08-HELP-Committee-Letter-to-Teva.pdf.

Rather than heed this warning, Teva re-certified the propriety of the 42 patent-listings identified in the warning letter, including each of the five patents listed for ProAir HFA that Teva asserts in this case.[14] Moreover, Teva re-certified those Orange Book listings despite the underlying device patents' failure to mention any drug at all in their claims. According to Amneal's counterclaims, Teva is using these improper Orange Book listings to restrict competition and delay Amneal from making less expensive generic inhalers available to the American public.[15]

The FTC submits this amicus brief because device patents improperly listed in the Orange Book can undermine fair competition, shutting out generics from the market and depriving Americans of access to lower-cost drugs.[16]

BACKGROUND

I. The Statutory and Regulatory Framework

Congress passed the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act,[17] with the aim of "balanc[ing] two

[14] *See* Teva Warning Letter, *supra* note 11; Norton Warning Letter, *supra* note 11.
[15] Amneal Countercl., ECF No. 12 ¶¶ 101-05; 120-25.
[16] As the FTC stated in its policy statement, the Commission will "use all its tools to halt unlawful business practices that contribute to high drug prices." FTC Orange Book Policy Statement, *supra* note 9. In filing this amicus brief, the FTC does not disclaim or waive its right to bring an enforcement action against Teva or any other company that the FTC believes may continue to improperly list patents in the Orange Book.
[17] Pub. L. No. 98-417, 98 Stat. 1585 (1984).

competing interests."[18] On the one hand, the Hatch Waxman Act "encourag[es] research and innovation" by protecting brand drug companies' patent interests associated with drugs approved through the NDA.[19] On the other, the Act seeks to facilitate getting lower-cost "generic drugs on the market in a timely fashion"[20] through mechanisms like the abbreviated new drug application (ANDA), which provides an expedited pathway for approval of generic drugs.[21]

The Hatch-Waxman framework includes provisions "that encourage the quick resolution of patent disputes" for certain types of patents.[22] The Hatch-Waxman amendments and FDA regulations instruct brand manufacturers to submit information about certain patents for their NDA products to the FDA for publication in a compendium entitled "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly referred to as the "Orange Book."[23] Listing a patent in the Orange Book can be extremely valuable because it gives brand

---

[18] *In re Lantus Direct Purchaser Antitrust Litig.*, 950 F.3d 1, 5 (1st Cir. 2020) (citing Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 68 Fed. Reg. 36676 (June 18, 2003)

[19] *Id*.

[20] *Id.* at 11 (citing 68 Fed. Reg. at 36676).

[21] *See* 21 U.S.C. § 355(j).

[22] *AbbVie*, 976 F.3d at 339.

[23] *See Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405-6 (2012).

manufacturers the power to trigger an automatic delay of FDA approval of competing generic products, generally for 30 months.

When a drug company seeks to market a generic version of a brand drug for which there are patents listed in the Orange Book, the company must provide a "certification" for each listed patent "which claims the listed drug . . . or which claims a use for such listed drug for which the applicant is seeking approval."[24] For non-expired patents, the generic company can file a "paragraph IV" certification asserting that the brand company's patent is invalid or will not be infringed by the generic drug.[25] Notice of the certification triggers an immediate right for the brand manufacturer to sue for infringement.[26] When a brand manufacturer brings such an infringement suit within 45 days after receiving notice for a patent that was submitted to FDA prior to the submission of the ANDA, as Teva did here, the FDA's approval of the generic manufacturer's ANDA is automatically stayed for

[24] 21 U.S.C. 355(j)(2)(A)(vii); *see also* 21 C.F.R. § 314.95(a).

[25] *See* 21 U.S.C. § 355(j)(2)(A)(vii). If the generic is not contending the patents are invalid or not infringed, it would simply file a "paragraph III" certification signifying it will wait to come to market until patent expiry. *See id*.

[26] There is no right to file an infringement suit in response to a paragraph IV certification if the patent was obtained by fraud on the U.S. Patent and Trademark Office or if the infringement suit would be objectively baseless. *See*, *e.g.*, *AbbVie Inc.*, 976 F.3d at 361 ("[W]e must not immunize a brand-name manufacturer who uses the Hatch-Waxman Act's automatic, 30-month stay to thwart competition. Doing so would excuse behavior that Congress proscribed in the antitrust laws.").

30 months.[27] Unlisted patents can still be enforced after the generic product launches.[28]

Given the significant consequences of listing a patent in the Orange Book, Congress put strict limits on the types of patents that may be listed. The Hatch-Waxman Act included Orange Book listing provisions that require brand manufacturers to submit listing information for specific types of patents.[29] For over two decades, FDA regulations have further specified that patents eligible for listing "consist of drug substance (active ingredient) patents, drug product (formulation and composition) patents, and method-of-use patents."[30] More recently, Congress enacted the Orange Book Transparency Act of 2020 (OBTA), which amended the listing provisions to state that a patent should be listed only if a "claim of patent infringement could reasonably be asserted" and the patent:

> (I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or

[27] 21 U.S.C. § 355(j)(5)(B)(iii). If the patent is held infringed, that stay of approval is automatically extended until the patent's expiration date; *compare eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 390-1 (2006) (holding prevailing patent plaintiff must normally meet traditional four-factor test to obtain permanent injunction).

[28] *See Bayer AG v. Biovail Corp.*, 279 F.3d 1340, 1350 (Fed. Cir. 2002) (denying collateral estoppel because "infringement under [35 U.S.C] § 271I(2)(A) by submission of an ANDA is not synonymous with infringement under § 271(a) by a commercial product").

[29] Pub. L. No. 98-417, Stat. 1585.

[30] 21 C.F.R. § 314.53(b)(1) (2003).

> (II) claims a method of using such drug for which approval is sought or has been granted in the application.[31]

Further, the listing provisions provide that information on patents that do not meet these requirements "shall not be submitted."[32]

NDA holders have a responsibility to ensure that Orange Book patent listings meet the statutory requirements. The FDA considers its role in this listing process to be "purely ministerial."[33] It does not "police the listing process by analyzing whether the patents listed by NDA applicants actually claim the subject drugs or applicable methods of using those drugs."[34]

Although the FDA does not independently evaluate the patents submitted for listing in the Orange Book, it provides a process under which any person may "dispute[] the accuracy or relevance of patent information submitted."[35] Under that process, the FDA relays the dispute statement to the brand manufacturer. The brand manufacturer must respond within 30 days by instructing the FDA to delist the patent or amend the patent information, or by re-certifying under penalty of

---

[31] 21 U.S.C. § 355(b)(1)(A)(viii).
[32] *Id*. § 355(c)(2).
[33] *Organon Inc. v. Mylan Pharms., Inc.*, 293 F. Supp. 2d 453, 458-59 (D.N.J. 2003); *see also* U.S. Food & Drug Admin., Report to Congress: The Listing of Patent Information in the Orange Book, at 5 (Jan. 2022). https://www.fda.gov/media/155200/download ("FDA serves a ministerial role with regard to the listing of patent information").
[34] *Apotex v. Thompson*, 347 F.3d 1335, 1349 (Fed. Cir. 2003).
[35] 21 C.F.R. § 314.53(f).

perjury the propriety of the listings.[36] The FDA does not assess or take any other action on the dispute and will not change or remove the Orange Book listing unless the brand manufacturer instructs the FDA to do so in its response.[37]

In 2003, Congress authorized generic manufacturers that are sued for infringement of Orange Book-listed patents to bring a counterclaim seeking to remove the listing.[38] In addition to this delisting counterclaim, courts and the FTC have long recognized (both before and after the adoption of the delisting counterclaim provision) that improper Orange Book listings can also be actionable under the antitrust laws.[39] The FDA supports the FTC's efforts to examine whether brand drug companies are impeding generic drug competition by improperly listing patents in the Orange Book.[40]

---

[36] *See id.*

[37] *See id.*

[38] *See* 21 U.S.C. § 355(j)(5)(C)(ii)(I).

[39] *See, e.g.*, *Lantus*, 950 F.3d at 6-7, 15 (finding improper listing of component device patent may support Section 2 Sherman Act claim); *In re Loestrin 24 Fe Antitrust Litig.*, 433 F. Supp. 3d 274, 315 (D.R.I. 2019) (ruling "sham Orange Book listing claim" under Section 2 of the Sherman Act may proceed to trial); *In re Remeron Antitrust Litig.*, 335 F. Supp. 2d 522, 531 (D.N.J. 2004) ("there exists no regulatory scheme [for Orange Book listings] so extensive as to supplant antitrust laws"); *see also* FTC Study on Generic Drug Entry Before Patent Expiration, *supra* note 6, at 1; FTC Orange Book Policy Statement, *supra* note 9, at 1.

[40] *See* FTC Press Release re: Orange Book Policy Statement, *supra* note 9.

II. Teva Continues to Improperly List Patents in the Orange Book—Including the Asserted Patents—Despite FTC Staff Warnings

In November 2023, the FTC's Bureau of Competition sent letters to ten brand manufacturers informing them that FTC staff have opted to use the FDA's process to dispute over 100 Orange Book listings.[41]

In response, four brand drug manufacturers requested that the FDA remove from the Orange Book virtually all their patent listings identified by the FTC.[42] Several of those companies delisted asthma inhaler device patents and device component patents with claims that resemble the asserted patents in this case (i.e., device or device component patents that do not mention the active ingredient or the drug product that is the subject of the NDA in the patent claims).[43]

---

[41] FTC Press Release re: Improper Orange Book Listings, *supra* note 10.

[42] *See* U.S. Food & Drug Admin., *Patent Listing Disputes* (current through Mar. 8, 2024), https://www.fda.gov/media/105080/download (noting changes in the patent listings for Kaleo Inc., Impax Laboratories LLC, GlaxoSmithKline Intellectual Property Development Limited, and Glaxo Group Limited). All told, these four manufacturers voluntarily delisted fourteen patents across six NDAs, with one patent being listed for three different applications.

[43] For example, GSK removed listings for patents on an "actuation indicator" (U.S. Patent No. 7,500,444), a "dose counter for use with a medicament dispenser" (U.S. Patent No. 8,113,199), a "medicament dispenser" (U.S. Patent No. 8,161,968), and a "manifold for use in a medicament dispenser" (U.S. Patent No. 8,534,281). *Compare* Letter from Rahul Rao, Dep. Dir., Bur. Competition, Fed. Trade Comm'n to GlaxoSmithKline Intell. Prop. Dev. Ltd (Nov. 7, 2023), https://www.ftc.gov/system/files/ftc_gov/pdf/glaxosmithkline-orange-book.pdf, *and* Letter from Rahul Rao, Dep. Dir., Bur. Competition, Fed. Trade Comm'n to Glaxo Group Ltd (Nov. 7, 2023), https://www.ftc.gov/system/files/ftc_gov/pdf/glaxo-group-orange-book.pdf, *with*

Teva, however, did not delist or amend any of the 42 patent-listings disputed by the FTC, including the asserted patents in this case.[44] Each of the asserted patents were listed in the Orange Book during the period from 2012 to 2022.[45] The patents are device or device component patents that claim a dose counter or an inhaler that includes a dose counter.[46] On their face, none of these patents mention any drug in their claims, much less the active ingredient in ProAir HFA, albuterol sulfate.[47] Notably, the patent covering albuterol sulfate expired in 1989.[48]

Patent No.	Patent Title	List Date
8,132,712	Metered-dose inhaler	Mar. 27, 2012
9,463,289	Dose counters for inhalers, inhalers and methods of assembly thereof	Nov. 8, 2016
9,808,587	Dose counter for inhaler having an anti-reverse rotation actuator	Nov. 16, 2017
10,561,808	Dose counter for inhaler having an anti-reverse rotation actuator	Mar. 19, 2020
11,395,889	Dose counter for inhaler having an anti-reverse rotation actuator	Aug. 19, 2022

U.S. Food & Drug Admin., *Patent Listing Disputes*, *supra* note 42, and *Delisted Patents*, U.S. Food & Drug Admin., https://www.accessdata.fda.gov/scripts/cder/ob/search_patent.cfm?listed=delisted (last updated Mar. 20, 2024).

[44] *Compare* Teva Warning Letter, *supra* note 11 and Norton Warning Letter, *supra* note 11 *with* U.S. Food & Drug Admin., *Patent Listing Disputes*, *supra* note 42.

[45] Pl.'s Am. Compl., ECF No. 7, Exs. A-E.

[46] *See id.*

[47] *See id.*; *see also* Orange Book (44th ed. 2024), *supra* note 2, at ADA 7(listing active ingredient of ProAir HFA as albuterol sulfate).

[48] Orange Book AD 6 (7th ed. 1987) (referencing U.S. Patent No. 3,644,353) (on file with Hyman, Phelps, & McNamara PC, *The Orange Book Archives, 1987, 7th Ed.*, https://thefdalawblog.com/wp-content/uploads/2020/06/OB-Annual-1987-7th-Ed.pdf).

Each of the asserted patents is also listed in the Orange Book for other Teva products.[49] For example, Teva has listed U.S. Patent No. 10,561,808 on a dose counter in the Orange Book for *21 different approved drugs*, many of which contain entirely different active ingredients from ProAir HFA.[50]

Despite receiving warning letters from the FTC's Bureau of Competition, Teva continues to list device and device component patents that, on their face, do not mention any drug in their claims. As a result, Teva can trigger—and here, has in fact triggered—a 30-month stay that blocks competition from less expensive generic inhalers solely based on these patents. In this case, Amneal submitted its ANDA seeking approval to market a generic version of ProAir HFA on August 24, 2023, and alleges that absent the 30-month stay, it could launch its less expensive competitor asthma inhaler as early as this summer.

ARGUMENT

The FTC believes this Court should grant Amneal's motion for a judgment on the pleadings as to counterclaim counts 1-5 regarding Teva's improper Orange Book listings. To aid the court in its analysis of the other federal law counterclaims, the FTC also explains how improper Orange Book listings harm

[49] Amneal Countercl., ECF No. 12 ¶ 86.
[50] *See* Orange Book (44th ed. 2024), *supra* note 2, at ADA 7, 39-40, 178-188.

fair competition and can trigger antitrust liability, and why *Trinko* does not apply to Amneal's counterclaims.

I. Drug Manufacturers Cannot Lawfully List Device Patents That Are Not Limited to Either the Active Ingredient or the Approved Product

The statutory listing provisions and related regulations require that, to be properly listed in the Orange Book, a patent must "claim[] the drug for which the applicant submitted the [NDA]" and also be either "a drug substance (active ingredient) patent or a drug product (formulation or composition) patent."[51] Alternatively, the patent may claim a "method of using such drug for which approval is sought or has been granted in the application."[52] Here, Teva listed the asserted patents in the Orange Book as "drug product" patents,[53] and it is undisputed that these patents are not "drug substance" or "method of use" patents.

Teva contends that the asserted patents qualify for the second category—drug product. However, a device or device component patent that does not mention any drug in its claims is not a "drug product (formulation or composition) patent." Rather, FDA regulations instruct manufacturers to "submit information only on those patents that claim the drug product, as is defined in [21 C.F.R.] § 314.3, that

[51] 21 U.S.C. § 355(b)(1)(A)(viii). *See also* 21 C.F.R. § 314.53(b)(1).
[52] *Id.*
[53] Pl.'s Br. In Supp. Mot., ECF No. 28, at 6 ("There are nine unexpired patents listed in the Orange Book for ProAir® HFA, each listed as a drug product patent.") ("Teva Br.").

is described in the pending or approved NDA."[54] In turn, § 314.3 defines "drug product" as "a finished dosage form, e.g., tablet, capsule, or solution, *that contains a drug substance*, generally, but not necessarily, in association with one or more other ingredients."[55] Together, these provisions mean that brand drug manufacturers may list as "drug product (formulation or composition) patents" only those that claim the finished dosage form containing the drug substance of the relevant NDA.[56] The asserted patents do not meet this criterion because they are device and device component patents untethered from any drug—much less the ProAir HFA albuterol sulfate formulation.[57]

As the FDA stated in its 2003 rulemaking on patent submissions and listing requirements, for drug product patent listings, "[t]he *key factor* is whether the patent being submitted claims the finished dosage form of the approved drug

[54] 21 C.F.R. § 314.53(b)(1).

[55] 21 C.F.R. § 314.3(b) (emphasis added).

[56] 21 C.F.R. § 314.53(b)(1). The FDA's 2016 regulations made some "Technical Corrections to Regulatory Concepts" including modifying the text of § 314.53(b)(1) to reference "the drug product" instead of "a drug product." This was intended "to clarify that for patents that claim a drug product, the applicant must submit information only on those patents that claim the drug product, as is defined in § 314.3, that is described in the pending or approved NDA." *See* Abbreviated New Drug Applications and 505(b)(2) Applications, 81 Fed. Reg. 69580, 69631 (Oct. 6, 2016).

[57] Amneal argues device patents are not listable in the Orange Book. Def.'s Br. In Supp. Mot., ECF No. 48, at 14-21 ("Amneal Br."). Setting aside for present purposes whether device patents are *ever* listable, the FTC's view is that device and device component patents that do not claim the active ingredient or drug product that is the subject of the NDA are not listable.

product."[58] Here, the drug substance that was the subject of Teva's NDA for ProAir HFA is albuterol sulfate, and its finished dosage form is "metered aerosol."[59] The claims of the asserted patents mention neither albuterol sulfate nor the ProAir HFA albuterol sulfate metered aerosol. A comparison to one of Teva's actual formulation patents—which expired long ago—is illuminating. For example, claim 2 of U.S. Patent No. 5,695,743 claims "[a]n aerosol formulation comprising: (a) a therapeutically effective amount of [albuterol]; and (b) a propellant . . . comprising 1,1,1,2-tetrafluoroethane . . . ." This patent appears to have been properly listed, as this claim specifies the particular drug product—a metered aerosol formulation including the drug substance—for which Teva received approval. In contrast, the asserted patents do not even mention any elements of the formulation.

The First Circuit's decision in *In re Lantus Direct Purchaser Antitrust Litigation*, which similarly considered a device component patent and held its listing improper, is instructive.[60] In *Lantus*, the First Circuit considered an Orange Book listing for a combination drug/device product called Lantus SoloSTAR, a

[58] 68 Fed. Reg. at 36680 (emphasis added).
[59] *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, Product Details for NDA 021457*, U.S. Food & Drug Admin., https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=021457#22991 (last visited Mar. 21, 2024).
[60] 950 F.3d at 1.

"pre-filled drug delivery system" that dispenses insulin glargine to the patient—i.e., an insulin injector pen.[61] That patent claimed "aspects of a 'drive mechanism' that serves as a part of the SoloSTAR drug injector pen."[62] The claims of the patent listed in the Orange Book for SoloSTAR did not mention the active ingredient insulin glargine or the drug product for which the NDA was submitted, Lantus SoloSTAR.[63] The First Circuit held that Sanofi's patent was improperly listed, reasoning that "[t]he statute and regulations clearly require that only patents that claim the drug for which the NDA is submitted should be listed in the Orange Book" and a patent that "neither claims nor even mentions the [active ingredient] or the [approved drug], does not fit the bill."[64] The Teva listings at issue here are strikingly similar to those the First Circuit held improper in *Lantus*.

The Second Circuit recently followed *Lantus*'s reasoning in a case where a brand manufacturer listed patents claiming methods of treatment using a combination of two active ingredients, even though the relevant NDA product contained only one of those two active ingredients.[65] The Second Circuit concluded that under *Lantus* "[a] patent claim that fails to explicitly include the

---

[61] *Id.* at 4, 7.
[62] *Id.* at 5.
[63] *Id.* at 10.
[64] *Id.*
[65] *United Food & Com. Workers Loc. 1776 & Participating Emps. Health & Welfare Fund v. Takeda Pharm. Co. Ltd.* (*Actos*), 11 F.4th 118, 127, 134-35 (2d Cir. 2021).

drug actually makes *neither* type of claim on the drug" permitted under the listing provisions.[66]

Teva's other arguments that its patents are properly listed are unavailing. First, Teva contends that the OBTA undermined *Lantus* by adding "component" or "composition" in ways that changed the meaning of § 355.[67] The OBTA did no such thing. Each instance of "component" in § 355 was already included in the statute before OBTA was enacted.[68] And "composition" was added to the listing provisions only to further specify the *limits* on the scope of listable patents—codifying limits that existed in FDA regulations (but not the statute) pre-OBTA.[69]

Second, Teva argues that even though the asserted patents do not claim the drug substance listed in the NDA (albuterol sulfate), or even the drug product listed in the NDA (ProAir HFA Inhalation Aerosol), the Court should find its Orange Book listings proper because "[t]he Listing Statute Broadly Requires Listing All Patents that 'Claim the Drug,'" and the asserted patents purportedly "read on" the ProAir HFA inhaler—meaning that the ProAir HFA's inhaler meets each claim element of at least one claim of the asserted patents.[70] But Teva's

---

[66] *Id.* at 134-35 (citing *Lantus*, 950 F.3d at 8).
[67] Teva Br., ECF No. 28, at 13-14 (citing 21 U.S.C. §§ 355(b)(1)(A)(ii), (iii), (v), (viii).
[68] 21 U.S.C.S. §§ 355(b)(1) (LexisNexis 2019); *see also* Amneal Br., ECF No. 48, at 25.
[69] 21 U.S.C. § 355(b)(1)(A)(viii)(I); *cf* 21 C.F.R. § 314.53(b)(1) (2003).
[70] Teva Br., ECF No. 28, at 9, 14-16.

argument ignores the statutory text. Even assuming *arguendo* that the ProAir device can be considered a part of the "drug," under the statutory text, it is not a sufficient condition for proper listing that the patent "claims the drug." The statutory text allows only listing of a patent that "claims the drug . . . *and* is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent," or else claims an approved method of using the drug.[71] Here, Teva's device and device component patents are none of those three types.[72]

Third, Teva argues that "patents claiming drug products *or their components* must be listed in the Orange Book."[73] Teva claims that the definition of "dosage form" in 21 C.F.R. § 314.3 takes into account "such factors" as "[t]he way the product is administered" and "[t]he design features that affect frequency of dosing;" thus, Teva argues, it must list "patents covering any of the components . . . that contribute" to ProAir HFA's "finished dosage form" if they "relat[e] to 'the way the product is administered' and 'design features that affect frequency of dosing.'"[74] According to Teva, these include device and device component patents.

---

[71] 21 U.S.C. § 355(b)(1)(A)(viii)(I) (emphasis added).

[72] Teva cites *Apotex*, 347 F.3d at 1343-44 for its dictum that "[t]he listing decision thus requires what amounts to a finding of patent infringement, except that the 'accused product' is the drug that is the subject of the NDA." Teva Br., ECF No. 28, at 21. But that statement only occurred in the Court's analysis of its subject-matter jurisdiction, and in any event is no longer accurate in view of the OBTA amendments to the listing provisions.

[73] Teva Br., ECF No. 28, at 16 (emphasis added).

[74] *Id*. at 16-17.

In the FTC's view, this argument stretches the FDA's guidance well beyond a fair reading. As explained above (at 19), the FDA's guidance on whether to list a "drug product" patent stated the "*key factor* is whether the patent being submitted *claims* the finished dosage form."[75] Teva offers no authority or even explanation for widening the FDA's guidance to allow listing of device or device component patents that "contribute" in some way to the finished dosage form (rather than claiming it), or that "relat[e]" to the factors the FDA uses to determine a drug's dosage form.[76]

Indeed, in *Lantus*, the First Circuit rejected virtually the same argument that Teva now makes. There, Sanofi argued it could list its device component patent—claiming the drive mechanism of an insulin injector pen—because it was required to list patents on "integral components" of the approved drug product.[77] Noting a "gap between [Sanofi's] reading of the law and its filing of a patent that does not claim the listed drug," the First Circuit concluded there was "nothing in the statute or regulations that welcomes such a further expansion of the already stretched statutory terms, whereby an integral part of an injector pen becomes the pen itself, and in turn is a drug."[78] The First Circuit ultimately held that the patent was

[75] 68 Fed. Reg. at 36680 (emphasis added).
[76] Teva Br., ECF No. 28, at 16-17.
[77] *Lantus,* 950 F.3d at 8.
[78] *Id.*

improperly listed because, even "assum[ing] for the sake of argument that the Lantus SoloSTAR is a drug under the statute, there is still a vital link missing: the '864 patent does not claim or even mention the Lantus SoloSTAR."[79] The same logic applies here.[80]

Under Teva's reading of the statute, drug companies could list any patent—and obtain a 30-month stay of FDA approval of a generic competitor—where the patent covers even one minor component of a drug-device combination product. The limits Congress imposed on Orange Book listings reflect a desire to avoid such an absurd result, in which patents on even minor device components trigger a stay of FDA approval and delay competition from less expensive generic drug products. Indeed, Teva's interpretation is inconsistent with the language of the listing provisions and would impermissibly render the "drug substance" category in the

[79] *Id.*

[80] Teva briefly argues that any patent not expressly excluded in the listing regulation may be listed. Teva Br., ECF No. 28, at 17 *quoting* 21 C.F.R. § 314.53(b)(1) ("Process patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates are not covered by this section, and information on these patents must not be submitted to FDA.") (emphasis omitted). This sweeping argument lacks merit for the reasons identified by Amneal. Amneal Br., ECF No. 48, at 18 n.7. In addition, 21 C.F.R. § 314.53(b) imposes numerous requirements for listing drug substance, drug product, and method-of-use patents that Teva's argument would read out of the regulation by collapsing all of § 314.53(b) into its final sentence. Teva's argument would similarly make redundant the OBTA's adoption of the "drug substance" and "drug product" requirements in 21 U.S.C. § 355(b)(1)(A)(viii)(I).

listing provisions surplusage.[81] Specifically, if any patent on a "component" of the drug product—including the active ingredient—is listable as a drug product patent, then there would be no reason to have a separate "drug substance (active ingredient)" category.[82] The active ingredient is undoubtedly a "component" of the "drug product," along with the inactive ingredients.[83] Thus, the existence of a separate category of "drug substance" for the active ingredient indicates that "drug product" patents are not listable unless they claim the entire drug product, not just components.

In short, the Hatch-Waxman Act does not authorize the listing of the asserted patents because they do not mention any drug in their claims and are therefore not "drug product (formulation or composition) patent[s]" under the listing provisions, as Teva claims.

II. Improper Orange Book Patent Listings Harm Competition

Improper Orange Book listings harm competition by deterring and delaying entry of lower-cost generics. As discussed, the Hatch-Waxman framework gives brand drug manufacturers with patents listed in the Orange Book the ability to

---

[81] *Arlington Cent. Sch. Dist. Bd. of Educ. v. Murphy*, 548 U.S. 291, 299 n.1 (2006) (statutory interpretation presumes that "statutes do not contain surplusage").

[82] 21 U.S.C. § 355(b)(1)(A)(viii).

[83] *See Ben Venue Lab. v. Novartis Pharm. Corp.*, 10 F. Supp. 2d 446, 458 (D.N.J. 1998) ("There can therefore be no serious question that, under 21 C.F.R. § 314.53(b), a 'drug substance' or 'active ingredient' may be a 'component' of a drug product . . . .").

initiate patent infringement litigation against would-be generic competitors before the FDA approves their ANDAs, which can lead to a 30-month stay of approval, regardless of whether the patent is properly listable.[84] Purchasers, like patients, hospitals, and health plans, are harmed each day that competition is delayed beyond the point the FDA would have otherwise approved a generic challenger's ANDA product. These potential harms—both in terms of higher drug prices and patient health—are serious.

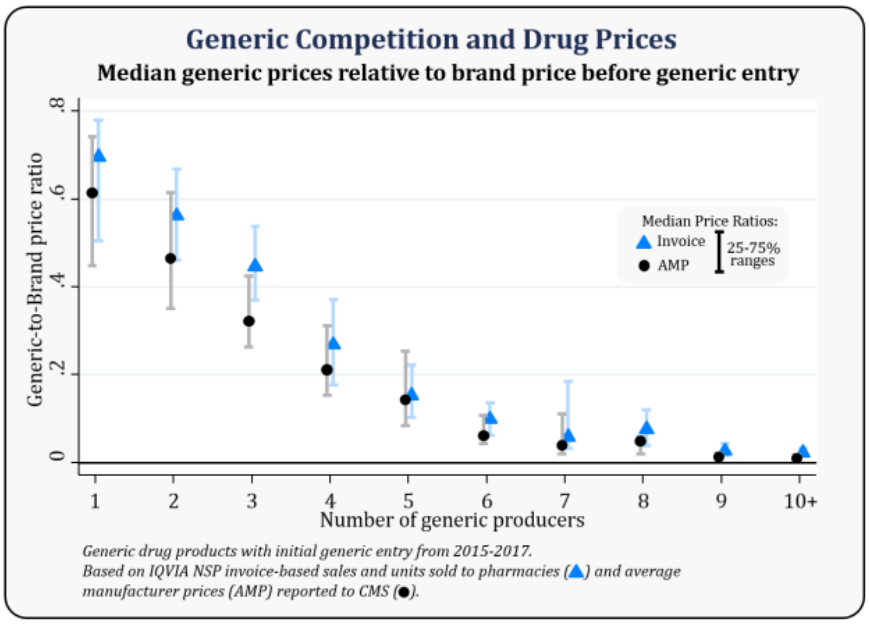
When generic drugs enter a market, prices tend to fall dramatically. The following graph from an FDA study illustrates the effects of increased competition on generic drug prices relative to the brand drug price before entry.[85] Researchers have found that with robust competition, most drug prices "eventually fall[] to 80–85% below the original brand-name cost."[86]

---

[84] This is true unless the generic competitor prevails in litigation sooner. *But see Lantus*, 950 F.3d at 4 ("[W]hile [the] thirty-month period may be shortened by resolution of the infringement action or order of the court [], the status quo, the allocation of burdens, and the life-span of patent litigation can all work against any such shortening.").

[85] U.S. Food & Drug Admin., Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices 2 (Dec. 2019), https://www.fda.gov/media/133509/download.

[86] Robin Feldman et al., *Empirical Evidence of Drug Pricing Games—A Citizen's Pathway Gone Astray*, 20 Stan. Tech. L. Rev. 39, 46 (2017); *see also* Herbert Hovenkamp, *Antitrust and the Patent System: A Reexamination*, 76 Ohio St. L.J. 467, 491 (2015) ("[C]ompetition among generics drives prices to the competitive level," which can be "as little as 20% of pre-generic-entry prices.").



In this case, because the asserted patents have been listed in the Orange Book, Teva's suit has triggered the 30-month stay of approval on Amneal's ANDA product until February 2026.[87] If not for this 30-month stay, Amneal alleges the FDA could approve its ANDA product as early as next month, April 2024,[88] and pleads that if approved it could come to market as early as this summer.[89] Absent this Court granting judgment on the pleadings as to counterclaim counts 1–5 and ordering the asserted patents delisted, Amneal's product—and the price competition it would bring—may be delayed by nearly two years.[90]

[87] This is true unless Amneal prevails in this litigation sooner.
[88] Amneal Br., ECF No. 48, at 3.
[89] Amneal Countercl., ECF No. 12 ¶ 122.
[90] The entry of Amneal's product would also increase patient choice.

In addition to raising prices, delayed competition from improper Orange Book listings may in turn harm patient health. In 2018, the American Thoracic Society (ATS) issued a policy statement observing that the high cost of inhalers and other medicines for patients with asthma and COPD has led to higher out-of-pocket expenses and harmed patient health.[91] Based on its review of the academic literature, the ATS concluded that higher out-of-pocket expenses can increase stress, reduce medication adherence, and lead to worse health outcomes, including unnecessary hospitalizations.[92] The ATS also noted that these problems have been "exacerbated by a paucity of generic alternatives"—i.e., by a lack of competition.[93]

Improper Orange Book listings appear to be part of a widespread problem, particularly with inhaler device and device component patents. As explained above, the FTC's Bureau of Competition's November 2023 warning letters disputed over 100 Orange Book listings by ten brand drug manufacturers across 13 inhaler products and four epinephrine injector pens.[94] With respect to even just Teva alone, the letters disputed a total of 42 patent-listings across four inhaler

[91] Minal R. Patel et al., *Improving the Affordability of Prescription Medications for People with Chronic Respiratory Disease: An Official American Thoracic Society Policy Statement*, 198 Amer. J. of Respiratory & Critical Care Med. 1367 (2018).
[92] *Id.* at 1368.
[93] *Id.* at 1367.
[94] *See* FTC Press Release re: Improper Orange Book Listings, *supra* note 10.

products.[95] Additionally, a study published just last year examined all 53 asthma and COPD inhalers approved by the FDA from 1986 to 2020 and found that 39 of these products collectively listed 137 device patents in the Orange Book, the majority of which (105, or 77%) failed to reference an active ingredient.[96]

Further, improper Orange Book listings create barriers to entry that may deter generic competitors from entering the market in the first place. Faced with the prospect of a 30-month delay of FDA-approval, a generic competitor may forgo entry altogether, harming competition.

The revenue generated by brand drug companies from delays in competition caused by improper Orange Book listings and other practices can be significant. A recent academic study of FDA-approved asthma/COPD inhalers calculated the revenue generated by brand manufacturers before and after patents on the active ingredients expired.[97] As illustrated in the graph below, the study found that over

---

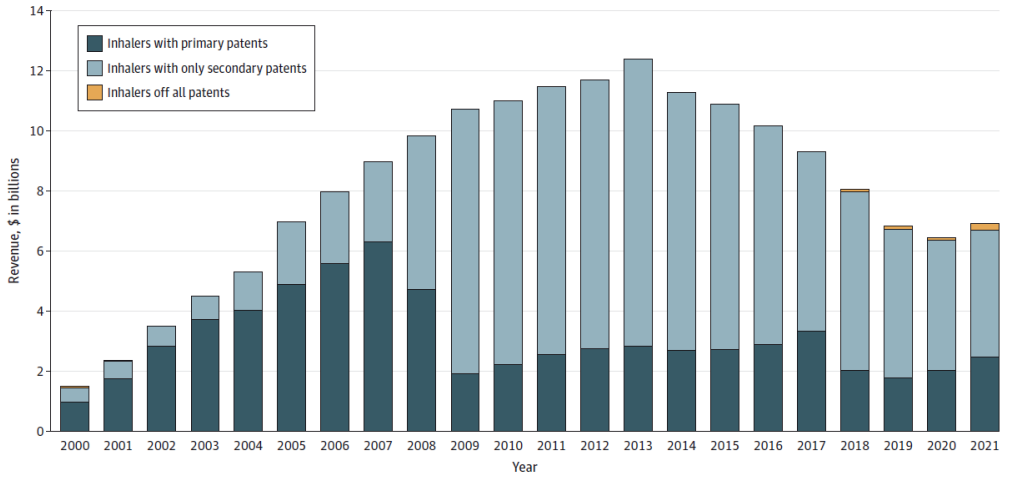
[95] *See* Teva Warning Letter, *supra* note 11; Norton Warning Letter, *supra* note 11.

[96] Brandon J. Demkowicz et al., *Patenting Strategies on Inhaler Delivery Devices*, 164 Chest 450, 452 (2023). This is consistent with a prior study that examined Orange Book patents on asthma/COPD inhalers, epinephrine injectors, and insulin injectors and concluded that 90% of the drug products studied were protected by device patents. *See* Reed F. Beall et al., *Is Patent "Evergreening" Restricting Access to Medicine/Device Combination Products?*, 11 PLOSE ONE 3 (2016).

[97] *See* William B. Feldman et al., *Manufacturer revenue on inhalers after expiration of primary patents, 2000-2021*, 329 J. Amer. Med. Assoc. 1, 3 (2023). This study did not measure the revenue obtained from delays in generic approval specifically due to improper Orange Book listings, but it demonstrates the

the 2000–2021 period, brand manufacturers generated $67.2 billion in revenue while their active ingredient patents were in effect compared with $110.3 billion after the active ingredient patents expired and the inhalers were protected only by later-filed secondary patents, including device and device component patents.[98]

Figure. Revenue Earned in the US on Brand-Name Inhaler Lines Approved by the US Food and Drug Administration, 2000-2021



III. Improper Orange Book Listings May Constitute Illegal Monopolization Under Section 2 of the Sherman Act

Contrary to Teva's arguments in its motion to dismiss, the FTC and courts have long recognized that improper submission of patents for listing in the Orange Book may constitute illegal monopolization—as well as an illegal course of monopolistic conduct—under section 2 of the Sherman Act.[99]

---

enormous value for brand drug manufacturers in delaying generic competition through any means—including obtaining 30 month stays through improper listings.

[98] *Id.* at 1.

[99] As the FTC's policy statement explains, improper Orange Book listings are also actionable under section 5 of the FTC Act, which prohibits unfair methods of

Monopolization requires proof of "the willful acquisition or maintenance of [monopoly] power as distinguished from growth or development as a consequence of a superior product, business acumen, or historic accident."[100] To establish a section 2 violation, a plaintiff must show "(1) that the defendant possesses monopoly power in the relevant market, and (2) that the defendant has acquired or maintained that power by improper means."[101]

Here, Teva seeks dismissal only with respect to the latter "improper means" element.[102] Demonstrating acquisition or maintenance of monopoly power by improper means requires proof that the defendant has engaged in anticompetitive conduct "to foreclose competition, to gain a competitive advantage, or to destroy a competitor."[103] As described above, improper Orange Book listings can foreclose competition and patient access to affordable medications by enabling brand companies to block generic competition generally for 30 months—regardless of whether the listed patent is valid or infringed by the competitor's product. Moreover, improper Orange Book listings can deter generic drug companies from

---

competition. *See* FTC Orange Book Policy Statement, *supra* note 9, at 5-6. There is no federal private right of action to enforce Section 5; this case focuses on Section 2 of the Sherman Act alone.

[100] *United States v. Grinnell Corp.*, 384 U.S. 563, 570-71 (1966).

[101] *Lantus*, 950 F.3d at 7 (quoting *Town of Concord v. Bos. Edison Co.*, 915 F.2d 17, 21 (1st Cir. 1990)) (additional citation and internal quotation omitted).

[102] *See* Teva Br., ECF No. 28, at 24.

[103] *Eastman Kodak Co. v. Image Tech. Servs., Inc.*, 504 U.S. 451, 482-83 (1992) (quoting *United States v. Griffith*, 334 U.S. 100, 107 (1948)).

entering a market at all, thereby foreclosing competition and depriving patients of lower-priced competing drugs. Courts (and the FTC) have consistently recognized that improperly listing patents in the Orange Book may constitute an improper means of maintaining or acquiring monopoly power—and they have done so both before and after 2003 when Congress enacted the counterclaim for a delisting injunction in 21 U.S.C. § 355(j)(5)(C)(ii).[104]

In this case, Amneal counterclaims that Teva improperly listed the asserted patents in the Orange Book, thus unlawfully maintaining its monopoly power.[105] As described above, these improper listings have enabled Teva to trigger the 30-month stay of approval, effectively delaying entry of Amneal's ANDA product

[104] *See Lantus*, 950 F.3d at 1, 7, 11-15 (reversing dismissal and holding allegations regarding improper listing of device patent could support actionable Sherman Act section 2 claim); *Actos*, 11 F.4th at 134-138 (affirming denial of motion to dismiss and remanding for consideration of whether brand drug manufacturer incorrectly listed patents in Orange Book causing antitrust harm); *Loestrin 24 Fe*, 433 F. Supp. 3d at 315 (ruling "sham Orange Book listing claim" may proceed to jury trial); *In re Gabapentin Pat. Litig*., 649 F. Supp. 2d 340, 360 n.23 (D.N.J. 2009) (recognizing improper Orange Book listing allegations could support monopolistic scheme allegations); *Remeron*, 335 F. Supp. 2d at 532 (allowing plaintiffs to present facts concerning improper listing in support of monopolistic scheme allegations); Decision & Order, *Biovail*, FTC Dkt. No. C-4060 (settling an action under the antitrust laws against Biovail Corporation for, among other things, wrongful Orange Book listing); FTC Study on Generic Drug Entry Before Patent Expiration, *supra* note 6 at App. H (discussing "three categories of patents that raise Orange Book listability questions"); FTC Orange Book Policy Statement, *supra* note 9.

[105] Amneal Countercl., ECF No. 12 ¶ ¶ 120-25, 134-270.

from as early as this summer to February 2026.[106] These facts, which at the motion to dismiss stage must be accepted, establish a plausible violation of section 2.

IV. The Narrow *Trinko* Exception Does Not Immunize Improper Orange Book Listings From Antitrust Scrutiny

Verizon Commc'ns, Inc. v. Trinko, LLP[107] cannot immunize Teva from antitrust liability for improper Orange Book listings. In *Trinko*, the Supreme Court declined to expand Section 2 of the Sherman Act to capture conduct that was "not a recognized antitrust claim under this Court's existing refusal-to-deal precedents,"[108] particularly where the federal and state regulatory "regime was an effective steward of the antitrust function."[109] The antitrust claims and the regulatory framework at issue here are nothing like those considered in *Trinko*. As explained below, *Trinko* is inapplicable because Amneal's counterclaims are not an expansion of antitrust law, the FDA does not directly police the Orange Book, and the statutory amendment to add a delisting counterclaim does not transform a patent enforcement framework into an antitrust regulatory scheme.

This Court rightly rejected Teva's argument, explaining that "there exists no regulatory scheme [for Orange Book listing] so extensive as to supplant antitrust

---

[106] *See supra* Background §§ I, II; Amneal Br., ECF No. 48, at 3; Amneal Countercl., ECF No. 12 ¶¶ 121-22, 130.
[107] 540 U.S. 398 (2004).
[108] *Id*. at 410.
[109] *Id.* at 413.

laws."[110] As Judge Hochberg explained, "[n]o authority has been cited to support the proposition that the antitrust laws have been superseded by the Hatch-Waxman Act or by FDA regulations. *Trinko* does not bar the instant antitrust claims."[111]

First, Amneal does not ask the Court to "recognize an expansion of the contours of §2" beyond existing precedents.[112] Courts have consistently recognized that lawsuits based on improperly listed Orange Book patents may constitute an "improper means" of maintaining or acquiring monopoly power.[113] Even before the Hatch-Waxman Act, courts recognized that improper use of a patent to exclude competitors can violate Section 2.[114]

Second, the FDA's ministerial role in Orange Book listings is nothing like the extensive scheme of Federal Communications Commission (FCC) regulation of telecommunications competition considered in *Trinko*. In *Trinko*, the local phone incumbent, Verizon, allegedly provided poor network access to prospective rivals,

---

[110] *Remeron*, 335 F. Supp. 2d at 531.

[111] *Id.* at 531. Other courts have similarly rejected attempts to extend *Trinko* to preclude antitrust claims in other contexts. *See, e.g., Steward Health Care Sys., LLC v. Blue Cross & Blue Shield*, 997 F. Supp. 2d 142, 153 n.6 (D.R.I. 2014) (rejecting argument that "the heavily regulated nature of health care markets makes it improper for courts to intervene on antitrust grounds," explaining "[w]hereas the telecommunications industry at issue in *Trinko* was the subject of extensive antitrust regulation, it cannot be said that the same level of antitrust-focused regulation exists in health care markets").

[112] *Trinko*, 540 U.S. at 412.

[113] *See supra* note 105.

[114] *See, e.g.*, *SmithKline Corp. v. Eli Lilly & Co.,* 575 F.2d 1056, 1065 (3rd Cir. 1978).

leaving them unable to consistently serve the phone customers they sought to take from Verizon. The Telecommunications Act of 1996 "sought to 'uproot' the incumbent [local phone company's] monopoly and to introduce competition in its place."[115] "Central to the scheme of the Act [was] the incumbent [phone company's] obligation … to share its network with competitors," along with "a complex regime for monitoring and enforcement" by the FCC.[116] The New York Public Service Commission imposed similar network sharing conditions.[117] After Verizon's competitors complained about its conduct,[118] New York and the FCC opened parallel investigations; within months, New York issued orders requiring Verizon to pay $10 million to its rivals, and Verizon paid $3 million under an FCC consent decree.[119]

The Supreme Court gave "particular importance" to this "regulatory structure designed to deter and remedy anticompetitive harm" when it declined the *Trinko* plaintiffs' request to expand Section 2.[120] In *Trinko*, the FCC—an agency

[115] *Trinko*, 540 U.S. at 402 (quoting *Verizon Communications Inc. v. FCC*, 535 U.S. 467, 488 (2002)).
[116] *Id.* at 401-02 (citations omitted).
[117] *Id.* at 398.
[118] *Id*. at 403.
[119] *Id.* at 403-04.
[120] *Id.* at 412.

with longstanding competition expertise and statutory enforcement authority[121]—and New York "provided a strong financial incentive for [Verizon's] compliance."[122] When Verizon failed to meet its obligations, the regulators responded quickly, "impos[ing] a substantial fine" and onerous, "*daily* reporting requirements" to ensure compliance.[123] Collectively, this regulatory "regime was an effective steward of the antitrust function."[124]

Here, however, the FDA's "purely ministerial" role with Orange Book patent listings is starkly different from the FCC's role in *Trinko*.[125] "The FDA's mission is to protect the public by ensuring that drugs are safe and effective," not to "resolve economic disputes about the coverage of patent claims."[126] And the

---

[121] *See Steward,* 997 F. Supp. 2d at 153 n.6 ("the telecommunications industry at issue in *Trinko* was the subject of extensive antitrust regulation"); *Competition Policy Division, Wireline Competition Bureau*, Fed. Commc'n Comm'n., https://www.fcc.gov/general/competition-policy-division-wireline-competition-bureau (last visited Mar. 20, 2024) ("Our primary mission is to foster competition…"); Judge Douglas Ginsburg & Josh Wright, *Reimagining Antitrust Institutions: A (Modest?) Proposal* (George Mason L. & Econ. Rsch. Paper No. 23-22, at 14, 2023) (forthcoming, Rev. L. Econ.) (explaining "[s]ome sectoral regulators also have sector-specific analogs to the [FTC] Section 5 authority to prevent 'unfair methods of competition.' Agencies with such authority include the FCC, over cable operators…").

[122] *Trinko*, 540 U.S. at 413 (citations omitted).

[123] *Id.*

[124] *Id.*

[125] *Organon*, 293 F. Supp. 2d at 458-59.

[126] *Remeron*, 335 F. Supp. 2d at 531-32 (quoting Fed. Defs.' Mem. in Opp'n to Pls.' Mot. for Prelim. Injunction, *Mylan v. Thompson*, 139 F. Supp. 2d 1 (D.D.C. 2001)).

FDA has stated that it "lack[s] the resources, authority, or expertise to police patent claims" that delay the entry of generic drugs.[127] As the Federal Circuit has explained, the FDA does not "police the listing process by analyzing whether the patents listed by NDA applicants actually claim the subject drugs or applicable methods of using those drugs."[128] The FDA supported the FTC's efforts to scrutinize improper Orange Book patent listings under the antitrust laws.[129]

Nor does the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) create a regulatory structure that supplants the need for the antitrust laws to address anticompetitive harm, as Teva asserts.[130] By its plain terms, the MMA merely provides a mechanism for courts to require delisting of improper Orange Book patents—i.e., an injunctive relief counterclaim—and does not limit or displace the availability of antitrust liability, including for damages.[131]

Specifically, Subclause I of the relevant provision established a counterclaim for an ANDA filer to seek removal of an improperly listed patent from the Orange Book during patent infringement litigation brought under the Hatch-Waxman

---

[127] Br. for the U.S. as Amicus Curiae, *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, No. 10-844, 2011 WL 3919720, at *17, 27 (U.S. Sept. 6, 2011); *see also Caraco*, 566 U.S. at 424 (noting "the FDA's determination that it cannot police patent claims.").

[128] *Apotex*, 347 F.3d at 1349.

[129] *See* FTC Press Release re: Orange Book Policy Statement, *supra* note 9.

[130] Teva Br., ECF No. 28, at 28.

[131] *See* Amneal Br., ECF No. 48, at 39-40 (quoting H.R. Rep. No. 108-391, at 836 (2003)).

Act.[132] Subclause II specifies that the "claim described in subclause (I)" may only be brought as a counterclaim to a patent infringement suit.[133] Nothing in the statute preempts, or even mentions, the well-established antitrust claims raised by Amneal here—which are claims authorized by the Sherman Act that in no way depend on the authority to bring "the claim described in subclause (I)" of the MMA.

Moreover, the MMA counterclaim does not offer any means to remedy the types of harm to competition from improper Orange Book listings that antitrust liability addresses. For one, the MMA counterclaim cannot lead to monetary damages; it may only correct the Orange Book listing and does not allow for any other remedy.[134] Additionally, the counterclaim arises only if and when a branded drug manufacturer sues a generic drug manufacturer for infringement of a product covered by an Orange Book listing. Thus, the counterclaim cannot address the chilling effect of improper patent listings that discourage would-be competitors from even attempting to enter the market—harming competition and consumers. Such a mechanism does not constitute a comprehensive antitrust regulatory regime.

---

[132] 21 U.S.C. § 355(j)(5)(C)(ii)(I) ("If an owner of the patent … brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information...").

[133] 21 U.S.C. § 355(j)(5)(C)(ii)(II) ("Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).").

[134] *See Id*. § 355(j)(5)(C)(ii)(II) (Applicants "not [] entitled to damages").

Indeed, even after the enactment of the MMA counterclaim, courts have repeatedly and consistently recognized that improper Orange Book listings can violate Section 2.[135] The FTC is not aware of any case extending *Trinko* to preclude antitrust liability for improper Orange Book listings. This Court should reject Teva's invitation to become the first. Notably, in a case alleging sham litigation under the Hatch Waxman Act, the Third Circuit rejected a branded drugmaker's *Noerr-Pennington* argument, holding that courts "must not immunize a brand-name manufacturer who uses the Hatch-Waxman Act's automatic, 30-month stay to thwart competition. Doing so would excuse behavior that Congress proscribed in the antitrust laws."[136] Courts have long recognized that antitrust exemptions are "strongly disfavored and have only been found in cases of clear repugnancy between the antitrust and regulatory provisions."[137] No such conflict exists here.

CONCLUSION

For the foregoing reasons, the Court should grant Amneal's motion for a judgment on the pleadings as to counterclaim counts 1-5 and order the asserted patents delisted. The Court should evaluate the issues consistent with the principles

[135] *See supra* note 105.
[136] *AbbVie Inc.*, 976 F.3d at 361.
[137] *Otter Tail Power Co. v. United States*, 410 U.S. 366, 372 (1973).

described above, including that improper Orange Book listings may cause substantial harm to competition and may violate the antitrust laws.

Dated: March 22, 2024

Respectfully submitted,

Hannah Garden-Monheit
Director, Office of Policy Planning

Henry Liu
Director, Bureau of Competition

Anisha Dasgupta
General Counsel, Federal Trade Commission

/s/ Bradley J. Vettraino
Bradley J. Vettraino
Ian Barlow
Rahul Rao
Anupama Sawkar
Matthew Frank
Clarke Edwards
Jordan Klimek
600 Pennsylvania Avenue N.W.
Washington, D.C. 20580
Telephone: (202) 386-2652

fact that need resolution so Amneal is not entitled to judgment as a matter of law.

3. Even if the Court denies Teva's Rule 12(b)(6) Motion, it should still deny Amneal's Rule 12(c) Motion

To the extent the Court denies Teva's Rule 12(b)(6) Motion because it adopts Amneal's interpretation of the Listing Statute and finds Amneal has plead sufficient factual allegations to state a claim for relief, the Court should still deny Amneal's Rule 12(c) Motion. Even under Amneal's incorrect interpretation of the statute, Amneal's Motion at best shows that there are claim construction issues concerning at least whether the Asserted Patents "claim[] the drug" and are "drug product (formulation or composition) patent[s]" under Amneal's interpretation. *See Jazz Pharms., Inc. v. Avadel Pharms. PLC*, 2021 WL 4860682, at *3 (D. Del. Oct. 19, 2021) (denying Rule 12(c) motion, in part, because "the vast majority of courts have held claim construction to be inappropriate on a motion under Rule 12"); *see, e.g.*, *Tolmar*, 2022 WL 13858026, at *6 (denying Rule 12(c) motion because movant's arguments depend on claim constructions, but claim construction proceedings had not yet occurred). The Court should deny Amneal's Rule 12(c) Motion at least to engage in claim construction proceedings if necessary to determine the scope of what the Asserted Patents claim.[22]

[22] In *Jazz Pharms., Inc. v. Avadel Pharms.*, No. 1-21-cv-00691 (D. Del.), the district court denied Avadel's Original Motion for Judgment on the Pleadings for its delisting counterclaims to engage in claim construction and discovery. (ECF No. 55). After claim construction, Avadel filed a Renewed Motion for Judgment on the

amneal

January 10, 2024

The Honorable Elizabeth Warren
309 Hart Senate Office Building
Washington, DC 20510

The Honorable Pramila Jayapal
2346 Rayburn House Office Building
Washington DC, 20515

Re: December 13, 2023 Correspondence Regarding Patent Listings

Dear Senator Warren and Representative Jayapal:

I write on behalf of Amneal Pharmaceuticals LLC (Amneal), a New Jersey-headquartered pharmaceutical company providing millions of American patients with accessible, essential medicines, powered by a robust U.S. generic medicines business and growing biosimilar and specialty businesses. We are the leading U.S.-domiciled company that manufactures accessible, essential medicines, with approximately 2,400 U.S.-based employees, and more than 270 FDA-approved generic products to date.

We appreciate your attention to the matters raised in your December 13, 2023 correspondence referencing the U.S. Federal Trade Commission (FTC) November 7, 2023 letter to Impax Laboratories LLC (Impax), a wholly owned subsidiary of Amneal Pharmaceuticals LLC. The FTC's letter concerned two patents associated with Adrenaclick® (epinephrine injection). Consistent with our mission to introduce competition to markets where it is otherwise lacking, Adrenaclick® was developed as an alternative to the EpiPen® autoinjector and has been available to American patients since 2003,[1] 15 years prior to FDA approval of generic versions of EpiPen® (epinephrine injection).

As you note, this product is approved under a new drug application (NDA), and is subject to the "patent listing" provisions under section 505(b) of the Federal Food, Drug, and Cosmetic Act that require NDA applicants to submit "the patent number and expiration date of each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that—(I) claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent; or (II) claims a method of using such drug for which approval is sought or has been granted in the application."[2]

[1] The product was approved in 2003 as Twinject®. Twinject® underwent labeling changes, which the U.S. Food and Drug Administration (FDA) approved in 2009, and became known as Adrenaclick®.
[2] 21 U.S.C. § 355(b)(1)(A)(viii).

In a good faith effort to comply with this statutory requirement given the regulatory guidance at the time, we submitted for listing in FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book) Patent No. 10166334 and Patent No. 7905352, the patents identified in the FTC's November 7, 2023 letter. However, we never have asserted the patents against a generic applicant for Adrenaclick® or any other party. Amneal reasonably believed the patents were properly listed. Numerous inquiries regarding whether these types of patents should be listed in the Orange Book have been made and regulators have declined to provide an opinion.[3] Upon receipt of the FTC's letter, we voluntarily requested delisting of both patents on November 21, 2023, which delisting is reflected in the Orange Book.[4] We also conducted a review of our portfolio of patent listings in the Orange Book and voluntarily delisted two additional patents listed for Twinject® (a discontinued version of our epinephrine auto-injector).[5] As with our patents covering Adrenaclick®, we never asserted these Twinject® patents against any third party. Thus, we have never triggered a 30-month stay in connection with the Adrenaclick® or Twinject® patents.

We share your concerns about the potential misuse of the patent system to stifle competition and inflate drug prices. In fact, we are currently involved in a litigation brought by Teva Branded Pharmaceutical Products R & D, Inc. (Teva) over our abbreviated new drug application filing for a generic version of Teva's ProAir® HFA (albuterol sulfate) inhalation aerosol product.[6] All of the patents asserted against us were listed in FTC's November 7, 2023 letter to Teva,[7] and the filing of this complaint by Teva triggered a 30-month stay of FDA final approval of our generic version until the litigation is resolved or the stay period expires. We recently informed FTC of this pending litigation along with our assertion of several antitrust and patent delisting counterclaims against Teva.

---

3 See e.g., Letter from the Centers for Drug Evaluation and Research, Food and Drug Administration, to GlaxoSmithKline, Wilmer Cutler Pickering Hale and Dorr LLP, Ropes & Gray LLP, Novo Nordisk Inc. and Finnegan, Henderson, Farabow, Garrett & Dunner LLP (June 1, 2020), available at https://www.regulations.gov/document/FDA-2005-A-0476-0006 (last accessed on Jan. 10, 2024). See also *Listing of Patent Information in the Orange Book; Establishment of a Public Docket*, Docket No. FDA-2020-N-1127, 85 FR 33169 (June 1, 2020), available at https://www.federalregister.gov/documents/2020/06/01/2020-11684/listing-of-patent-information-in-the-orange-book-establishment-of-a-public-docket-request-for, (last accessed on Jan. 10, 2024).

4 See Orange Book Delisted Patents, available at https://www.accessdata.fda.gov/scripts/cder/ob/search_patent.cfm?listed=delisted (last accessed on Jan. 10, 2024).

5 See Orange Book Patent Listing Disputes, available at https://www.fda.gov/media/105080/download?attachment (last accessed on January 10, 2024).

6 *Teva Branded Pharmaceutical Products R&D, Inc., Norton (Waterford) Limited, and Teva Pharmaceuticals USA, Inc.* v. *Amneal Pharmaceuticals of New York, LLC; Amneal Ireland Limited; Amneal Pharmaceuticals LLC, and Amneal Pharmaceuticals Inc.*, U.S. District Court for the District of New Jersey, Case No. 2:23-cv-20964.

7 Letter to Teva Counsel, Teva Branded Pharmaceutical Products R&D Inc. fr. R. Rao, Dep. Dir., FTC Bureau of Competition re Improper Orange Book-Listed Patents for QVAR 40, ProAir HFA, ProAir DigiHaler (Nov. 7, 2023), available at www.ftc.gov/system/files/ftc_gov/pdf/teva-branded-pharma-orange-book.pdf (last accessed on Jan. 10, 2024).

Jurisdictional Update: Metered Dose Inhalers, Spacers and Other Accessories

FDA has received inquiries regarding the jurisdiction of metered dose inhalers (MDIs) and accessories to be used with MDIs, such as spacers, actuators, spacers incorporating actuators, dose counters and locking clips. The purpose of this jurisdictional update is to clarify the regulation of these products.

MDIs consist of a pressurized canister containing a drug substance and possibly excipients formulated with a propellant. The formulation is aerosolized through a valve fitted with an actuator (mouthpiece). FDA has concluded that MDIs are drug – device combination products. [1] Based on the agency's determination that the primary mode of action of MDIs is attributable to the drug component, the Center for Drug Evaluation and Research (CDER) has regulated these products under the new drug provisions of the Federal Food, Drug, and Cosmetic Act (the act). This jurisdiction document applies equally to dry powder inhalers.

FDA has received marketing applications covering a variety of accessories intended to be used with MDIs. Many such accessories are "stand-alone" units intended for general use, i.e., they are not provided with or labeled for use in combination with a specific MDI. These products are ordinarily added to CDER-approved MDIs rather used to replace a component of an MDI. When FDA has determined that using the accessory would not alter the safety or efficacy of any MDI regardless of the MDI with which it is used, then the accessory labeling has not limited the use of the accessory to a specific MDI. FDA has ordinarily concluded that such accessories are devices. They have been regulated separately from the MDI by the Center for Devices and Radiological Health (CDRH) under the device provisions of the act. [2] Examples of specific jurisdictional determinations that have been made include the following:

"Stand-alone" Spacers are added to actuators of MDIs. They are essentially hollow tubes through which the aerosol cloud passes to reach the patient, but they are not necessary to deliver aerosolized drug to the patient. They can be "universal" in that they fit many different MDIs and do not replace any components of an approved MDI. These stand-alone spacers ordinarily are not labeled for use with a specific MDI.

Spacers will alter drug delivery characteristics to some extent, but do not specifically modify the approved drug product. CDRH has regulated spacers under the device provisions of the act since the products first became available. Because of this long experience, FDA believes that the safe and effective use of an MDI with a spacer does not ordinarily require that the spacer be labeled for use with a specific MDI. Therefore, CDRH has ordinarily regulated general use spacers under the device provisions of the act.

Locking clips are intended to prevent accidental actuation of the drug while the MDI is in the patient's pocket, purse, etc. Ordinarily, locking clips are removed prior to use of the MDI, although some products permit emergency drug administration while the locking clip is still in place. Locking clips are not ordinarily expected to affect the safety and efficacy of the drug, and locking clip labeling ordinarily does not limit the use of the clip to specific MDIs. In these circumstances, FDA has concluded that these accessories are devices. CDRH has regulated them under the device provisions of the act.

Some accessories are designed to replace a component of a previously approved MDI. In these cases, and in some cases where an accessory is designed to be added to a previously approved MDI, FDA has determined that the accessory must be studied and labeled for use with a particular MDI in order to ensure safe and

effective use of the MDI with the accessory. The intended use of these accessories creates a combination product through labeling. [3] In these cases, a lead Center has been assigned based on FDA's determination of the primary mode of action of the combination product. Examples of specific jurisdictional determinations that have been made include the following:

Actuators are an essential part of an MDI; the drug cannot be delivered to the patient without an actuator. Actuators also play a crucial role in the delivery characteristics of MDIs. The concept of a general use actuator is not appropriate because of this link to dosing performance; an actuator significantly affects the safety and efficacy of the drug, and must always be studied with a particular MDI drug. Therefore, replacement actuators have been determined to be device components of combination products. Based on FDA's determination that the primary mode of action of the combination product is attributable to its drug component, actuators have been regulated by CDER under the new drug provisions of the act [4]

Spacers incorporating actuators are designed to replace the actuator of an approved MDI. As with replacement actuators without a spacer, the concept of a general use actuator – spacer is not appropriate because an actuator must be studied with a particular drug. Therefore, actuator – spacers have been determined to be device components of combination products. Based on FDA's determination that the primary mode of action of the combination product is attributable to its drug component, spacer - actuators have been regulated by CDER under the new drug provisions of the act.

Dose counters or dose indicators count the number of doses administered by an MDI and display either numerically or by some other means the number of remaining doses, so that the patient will be aware when the drug canister has delivered its labeled contents. The force needed to actuate MDIs may vary from product to product by design, depending on factors such as the valve utilized in the product. For dose counters to provide accurate information, the force needed to actuate the counter must match the force needed to actuate the valve. Otherwise, "count-not-fire" and "fire-not-count" scenarios may occur. The "fire-not-count" scenario is particularly worrisome because the counter may indicate that the drug is available, when in fact the canister is empty.

For this reason, FDA believes that, in most cases, a dose counter must be designed to fit a specific MDI, and labeled for use with a specific MDI. Therefore, dose counters frequently have been determined to be device components of combination products. Based on FDA's determination that the primary mode of action of such a combination product is attributable to its drug component, dose counters have been regulated by CDER under the new drug provisions of the act. If a "universal" dose counter were developed, i.e., one where data demonstrate that the counter would work regardless of the characteristics of the MDI and would not alter drug delivery from the MDI, and so would not need to be labeled for use with a specific MDI, it would likely be considered a device and regulated under the device provisions of the act by CDRH.

For a determination whether a particular accessory to a MDI will be regulated as a device by CDRH or as the device component of a combination product by CDER, contact the Division of Anesthesiology, General Hospital, Infection Control, and Dental Devices, Anesthesiology and Respiratory Devices Branch at 301-796-5580. CDRH will consult with CDER and the Office of Combination Products (OCP) as necessary to make a determination whether the product is a device or the device component of a combination product.

Sponsors who disagree with the placement of a particular product in a particular Center may seek a formal assignment of the product from OCP through the Request for Designation (RFD) process. Further information about the RFD process is available at 21 CFR Part 3 (https://www.ecfr.gov/cgi-bin/text-idx?SID=0fdeb658f6ef1fc1d0344bb72fab9b74&mc=true&node=pt21.1.3&rgn=div5), and in the document

"Guidance for Industry and FDA: How to Write a Request for Designation (RFD)," available at the Combination Products (/combination-products) section of the FDA website. It is recommended that sponsors call the Office of Combination Products at 301-796-8930 to discuss their particular situation before submitting an RFD.

For further information about the review and regulation of metered dose inhalers and accessories see:

- Draft Guidance for Industry: Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products (/media/70851/download)
- Reviewer Guidance for Nebulizers, Metered Dose Inhalers, Spacers and Actuators (/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/reviewer-guidance-nebulizers-metered-dose-inhalers-spacers-and-actuators)

Footnotes

1. See 21 CFR § 3.2(e)(1) and (2). See also section VII.A.1(b) of the Intercenter Agreement between CDER and CDRH (/combination-products/classification-and-jurisdictional-information/intercenter-agreement-between-center-drug-evaluation-and-research-and-center-devices-and).

2. See section VII.A.1(a) of the CDER – CDRH Intercenter Agreement.

3. See 21 CFR § 3.2(e)(3).

4. Exception: Actuators that are added to the inspiratory limb of a ventilator circuit, rather than for standard oral inhalation, have been regulated as devices by CDRH under the device provisions of the act.

/ Drugs@FDA (/scripts/cder/daf/index.cfm)

Drugs@FDA: FDA-Approved Drugs

Home (index.cfm) | Previous Page

Abbreviated New Drug Application (ANDA): 203760
Company: PADAGIS US

EMAIL (MAILTO:?SUBJECT=DRUGS@FDA: FDA APPROVED DRUG PRODUCTS&BODY=HTTP://WWW.ACCESSDATA.FDA.GOV/SCRIPTS/CDER/DAF/INDEX.CFM?EVENT=OVERVIEW.PROCESS%26VARAPPLNO=203760)

Products on ANDA 203760

CSV | Excel | Print

Drug Name	Active Ingredients	Strength	Dosage Form/Route	Marketing Status	TE Code	RLD	RS
ALBUTEROL SULFATE	ALBUTEROL SULFATE	EQ 0.09MG BASE/INH	AEROSOL, METERED;INHALATION	Discontinued	None	No	No

Showing 1 to 1 of 1 entries

Approval Date(s) and History, Letters, Labels, Reviews for ANDA 203760

Original Approvals or Tentative Approvals

CSV | Excel | Print

Appx1422

Action Date	Submission	Action Type	Submission Classification	Review Priority; Orphan Status	Letters, Reviews, Labels, Patient Package Insert	Notes
02/24/2020	ORIG-1	Approval			**Letter (PDF) (https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/203760Orig1s000ltr.pdf)** **Review (PDF) (https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/203760Orig1s000.pdf)**	Label is not available on this site.

Showing 1 to 1 of 1 entries

Supplements

CSV Excel Print

Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, Patient Package Insert	Note
09/29/2020	SUPPL-2	Labeling-Package Insert		Label is not available on this site.

Showing 1 to 1 of 1 entries

/ Drugs@FDA (/scripts/cder/daf/index.cfm)

Drugs@FDA: FDA-Approved Drugs

Home (index.cfm) | Previous Page

Abbreviated New Drug Application (ANDA): 209954
Company: LUPIN

EMAIL (MAILTO:?SUBJECT=DRUGS@FDA: FDA APPROVED DRUG PRODUCTS&BODY=HTTP://WWW.ACCESSDATA.FDA.GOV/SCRIPTS/CDER/DAF/INDEX.CFM?EVENT=OVERVIEW.PROCESS%26VARAPPLNO=209954)

Products on ANDA 209954

CSV | Excel | Print

Drug Name	Active Ingredients	Strength	Dosage Form/Route	Marketing Status	TE Code	RLD	RS
ALBUTEROL SULFATE	ALBUTEROL SULFATE	EQ 0.09MG BASE/INH	AEROSOL, METERED;INHALATION	Prescription	AB2	No	No

Showing 1 to 1 of 1 entries

Approval Date(s) and History, Letters, Labels, Reviews for ANDA 209954

Original Approvals or Tentative Approvals

CSV | Excel | Print

Appx1425

Action Date	Submission	Action Type	Submission Classification	Review Priority; Orphan Status	Letters, Reviews, Labels, Patient Package Insert	Notes
08/24/2020	ORIG-1	Approval		STANDARD		Label is not available on this site.

Showing 1 to 1 of 1 entries

Supplements

CSV Excel Print

Action Date	Submission	Supplement Categories or Approval Type	Letters, Reviews, Labels, Patient Package Insert	Note
01/14/2021	SUPPL-4	Labeling-Container/Carton Labels, Labeling-Package Insert		Label is not available on this site.

Showing 1 to 1 of 1 entries

Therapeutic Equivalents for ANDA 209954

Generic Drugs Program Monthly and Quarterly Activities Report

ACTIONS BY MONTH	Oct-23	Nov-23	Dec-23	Jan-24	Feb-24	Mar-24	Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24	FY-2024
Approvals	57	51	53	56	52								269
First-Time Generics	4	4	4	6	7								25
First-Cycle Approvals	10	6	12	9	13								50
Imminent Actions	6	7	9	5	5								32
Tentative Approvals	16	17	11	17	11								72
First-Cycle Tentative Approvals	4	0	0	0	2								6
Imminent Actions	4	5	5	2	1								17
Complete Responses	141	137	131	136	144								689
Original ANDA Refuse to Receive	4	2	1	3	1								11
Standard	4	1	1	2	1								9
Priority	0	1	0	1	0								2
Original Acknowledgements	33	49	36	84	75								277
Withdrawals	8	27	10	14	10								69
Approved ANDA	0	18	0	8	0								26

ACTIONS BY MONTH	Oct-23	Nov-23	Dec-23	Jan-24	Feb-24	Mar-24	Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24	FY-2024
Unapproved ANDA	8	9	10	6	10								43
PAS Approvals	203	108	140	120	141								712
PAS Refuse to Receives	0	0	0	1	0								1
PAS Withdrawals	2	17	2	8	17								46
Information Requests	336	395	370	318	392								1811
Originals	135	169	175	173	192								844
Supplements	201	226	195	145	200								967
Discipline Review Letters	193	162	158	160	157								830
DMF Completeness Assessment	84	83	32	39	46								284
Reclassification of a Facility-Based Major CRL Granted	6	5	6	8	9								34
Reclassification of a Facility-Based Major CRL Denied	0	0	0	0	1								1
Pending ANDAs Awaiting FDA Action +	1477	1417	1475	1451	1427								--
ANDAs Awaiting Applicant Action ++	2056	2104	2100	2093	2109								--
Tentative Approvals +++	482	494	494	496	494								--
Complete Responses ++++	1574	1610	1606	1597	1615								--

SUBMISSIONS BY MONTH	Oct-23	Nov-23	Dec-23	Jan-24	Feb-24	Mar-24	Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24	FY-2024
ANDAs *	26	51	119	37	64								297
Complex Products	5	13	23	7	16								64
Amendments	211	194	213	210	198								1026
Major	55	52	69	67	57								300
Minor	50	46	59	73	65								293
Unsolicited	106	96	85	70	76								433
Requests for Reclassification of a Facility-Based Major CRL Amendment	4	6	12	15	15								52
Pre-Submission Facility Correspondence	11	5	5	3	7								31
Supplements	947	967	778	1100	1014								4806
CBE	818	832	640	948	891								4129
PAS**	129	135	138	152	123								677
DMF Payments	8	22	28	28	24								110
Controlled Correspondence ***	264	257	213	329	321								1384
Level 1	235	224	190	282	287								1218
Level 2	29	33	23	47	34								166
Controlled Correspondence Requests for Clarification	1	1	1	1	0								4

SUBMISSIONS BY MONTH	Oct-23	Nov-23	Dec-23	Jan-24	Feb-24	Mar-24	Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24	FY-2024
Product Development Meeting	7	4	9	5	10								35
Pre-Submission Meeting	0	0	0	0	0								0
PSG Teleconference	0	0	0	0	0								0
Pre-Submission PSG Meetings	0	0	0	0	0								0
Post-Submission PSG Meeting	0	0	0	0	0								0
Mid Cycle Review Meeting	1	0	0	0	1								2
Enhanced Mid Cycle Review Meeting	2	0	0	0	0								2
Post-CRL Clarification-Only Teleconference	3	7	11	1	5								27
Post-CRL Scientific Meeting	1	1	2	1	0								5

APPROVAL TIMES BY QUARTER *	Q1 (Oct - Dec 2023)	Q2 (Jan- Mar 2024)	Q3 (Apr - Jun 2024)	Q4 (Jul - Sept 2024)
Quarterly Mean Approval Times	39.84			
Quarterly Median Approval Times	26.07			
Quarterly Mean Tentative Approval Times	40.69			
Quarterly Median Tentative Approval Times	29.96			

Received: 22 January 2021 | Revised: 12 February 2021 | Accepted: 9 March 2021

DOI: 10.1111/cts.13046

ARTICLE

The timing of 30-month stay expirations and generic entry: A cohort study of first generics, 2013–2020

Sunand Kannappan[1] | **Jonathan J. Darrow**[2,3] | **Aaron S. Kesselheim**[2] | **Reed F. Beall**[1,2]

[1]Department of Community Health Sciences, Cummings School of Medicine, O'Brien Institute of Public Health, University of Calgary, Calgary, AB, Canada

[2]Program on Regulation, Therapeutics, and Law (PORTAL), Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA

[3]Department of Law and Taxation, Bentley University, Waltham, Massachusetts, USA

Correspondence
Reed F. Beall, Department of Community Health Sciences, Cummings School of Medicine, O'Brien Institute of Public Health, University of Calgary, Calgary, AB, Canada.
Email: reed.beall@ucalgary.ca

Funding information
Sunand Kannappan's work was funded by a studentship grant from the O'Brien Institute for Public Health at the University of Calgary. Dr. Beall's work is funded by an O'Brien Institute for Public Health catalyst grant for equitable drug innovation and access. Dr. Darrow and Dr. Kesselheim's work is funded by Arnold Ventures. Drs. Darrow and Kesselheim are also funded by a Novo Nordisk Foundation grant for a scientifically independent Collaborative Research Programme (grant NNF17SA0027784), by West Health, and by the Commonwealth Fund.

Abstract

Before the first generic version of a drug is marketed, patent litigation often occurs. The process begins when generic manufacturers notify the US Food and Drug Administration (FDA) of their intent to market a generic copy of a brand-name drug protected by patents, which they allege to be invalid or not infringed (called a Paragraph IV certification). Assuming the brand-name manufacturer responds with litigation within 45 days, a 30-month stay period is triggered, which bars the FDA from authorizing generic entry until the stay period expires or litigation is resolved in favor of the generic manufacturer. To understand whether 30-month stays delay generic entry, we examined the timing of major legal events leading to generic entry for a cohort of 46 generic drugs, including the timing of Paragraph IV certification filings, stay period expirations, the FDA approvals of generics, and generic product launches. We found Paragraph IV certifications were filed a median of 5.2 years after the brand drug's FDA approval. There was a median of 3.2 years between the stay period expiration and subsequent generic launch. Because stay periods generally expire well in advance of when generic entry typically occurs, 30-month stays are unlikely to delay the timing of generic entry. Patent litigation could begin even earlier, however, if litigation was allowed to start immediately following a brand-name drug's FDA approval; but by law currently, the soonest this can begin is 4 years after the brand drug's FDA approval.

Study Highlights

WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?

Before generic versions of new drugs reach the market, patent litigation often occurs. Once litigation has been initiated, a 30-month regulatory stay period is triggered that bars the US Food and Drug Administration (FDA) from approving the generic application until litigation resolves or the stay period expires.

WHAT QUESTION DID THIS STUDY ADDRESS?

What is the timing of key legal events in the regulatory approval process for generic drugs in relation to the eventual launch of the generic product?

WHAT DOES THIS STUDY ADD TO OUR KNOWLEDGE?

We identified the typical timing of the initiation of patent litigation and expiration of the 30-month stay period prior to the eventual launch of generic products. Litigation is often initiated as soon as legally possible (i.e., 4 years after the launch of the brand product), and stay periods typically expire well before generic entry occurs.

HOW MIGHT THIS CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?

Stay periods are unlikely to delay generic entry directly because stay expirations often occur well before the time of generic launch. Allowing the submission of generic drug applications immediately following a brand drug's FDA approval would facilitate earlier patent dispute resolution and prevent unnecessary delays in the anticipated generic product launch date.

INTRODUCTION

The process of introducing generic drugs into the US market is critically important for patients, because generic drugs increase competition, lower drug prices, and create an incentive for brand-name drugmakers to further innovate. Generic availability marks the end of the brand-name drug's period of market exclusivity, the length of which is often determined by the expiration of key patents. High prices charged during the exclusivity period allow brand-name manufacturers to recover research and development costs and earn a profit.

In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Act) to facilitate the approval of generic drugs. Under the Hatch-Waxman Act, generic drug manufacturers could obtain approval via a streamlined process that required much simpler and less expensive trials showing bioequivalence to the brand-name drug product. The new law restricted submission to the US Food and Drug Administration (FDA) of an application for a generic drug during the first 4 years after a branded drug's approval for the vast majority of drugs that are covered by patents (Figure 1), and provided for patent extensions of up to 5 years to account for time lost during the clinical trial and FDA approval process.

For patent-protected drugs, the generic manufacturer can assert that the patents are invalid or would not be infringed by the proposed generic version (called a "Paragraph IV certification"). If the brand-name manufacturer disagrees, it can initiate litigation. To incentivize earlier litigation, the brand-name manufacturer receives the benefit of a 30-month regulatory "stay" if it brings suit within 45 days of receivingnotice of the Paragraph IV certification, during which time the FDA cannot approve the generic drug. The law provides that the stay will not terminate until at least 7.5 years after the approval of the brand-name product, unless litigation resolves sooner or a court orders otherwise. The duration of the 30-month stay period was considered to be a reasonable amount of time for patent litigation to resolve.[1] If the stay expires before litigation ends, the FDA can approve the generic drug product and its manufacturer can launch "at-risk," entering the market while risking substantial damages if a court rules that the relevant patents are valid and infringed. At-risk launches are therefore likely only when the generic manufacturer is confident in the strength of its legal position in the ongoing litigation and when generic applications are far enough along to be reviewed and approved by the FDA.

The stay period has been a particular point of controversy because it links the drug regulatory system with the patent system. Supporters of the stay emphasize that it creates an incentive for patent litigation to begin (and therefore be resolved) sooner, because the stay is available only if the patent holder brings a legal suit within 45 days of receiving notice of the Paragraph IV challenge, before any actual infringement has occurred. Opponents of the stay argue that it leads to delays in generic entry when patents are later held to be invalid or not infringed. Linkage is also practiced in Australia, Canada, Japan, Mexico, Peru, Singapore, Taiwan, Ukraine, and Vietnam, and is being considered by China, Thailand, and Russia.[2] By contrast, in Brazil, Indonesia, the European Union, and Switzerland, among others, the patent and drug regulatory systems are kept separate so that drug regulatory bodies can approve applications for market entry from generic manufacturers once the products in question have satisfied regulatory requirements, irrespective of patent status. Following approval, disputes over intellectual property are resolved via the judicial system, and at-risk launches can more freely occur.

Almost 40 years after the Hatch-Waxman Act, policymakers continue to debate its strengths and weaknesses in facilitating generic entry,[3–8] but these debates often occur without systematic data on the various steps and legal milestones that must first occur. We therefore examined the timing of the major legal or regulatory events following Paragraph IV certification, the prevalence of stay periods, and the frequency with which generic products launch immediately after stay periods expire. One hypothesis was that stay periods would delay the timing of generic entry, which we sought to examine by calculating the time between stay expiration and generic launch.

METHODS

We tracked the timing of four major milestones leading to the availability of generic drugs for US patients, including the date of: (i) the original generic drug application submission to the FDA; (ii) expected stay expiration (absent earlier judicial resolution); (iii) FDA approval of the generic drug application; and (iv) generic drug launch. Finally, we

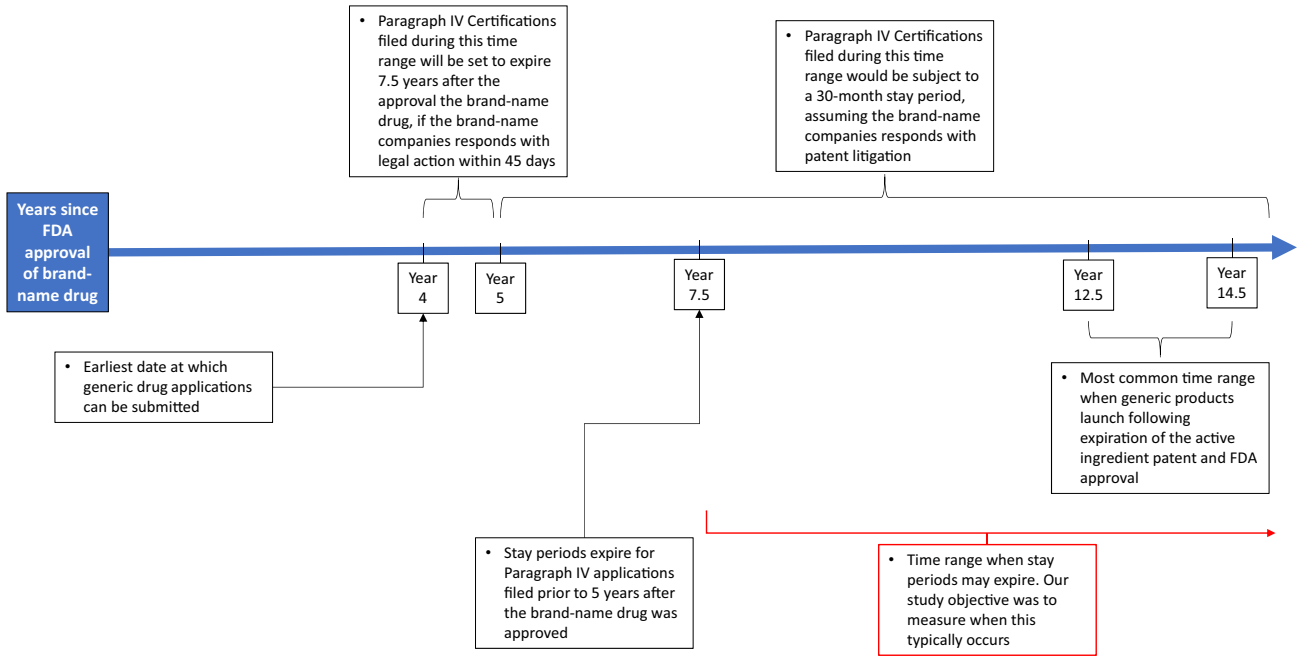


FIGURE 1 Key events and policies surrounding the processes leading to generic entry. *Notes:* The process of generic entry begins for more than half of new drugs with the filing of a Paragraph IV certification with the US Food and Drug Administration (FDA), which provides notice of a generic manufacturer's intent to market a copy of a new brand drug protected that is protected by patents that the generic manufacturer alleges to be invalid or not infringed. By law, the soonest this can begin is 4 years after the brand drug's FDA approval. If the Paragraph IV certification is filed between 4 and 5 years following the brand drug's FDA-approval and the brand manufacturer responds with patent litigation, a stay period is triggered that bars the FDA from authorizing generic entry until 7.5-years after the brand drug's FDA-approval or until litigation is resolved. If the Paragraph IV certification is filed 5 or more years following the brand drug's FDA-approval and the brand manufacturer responds with patent litigation, a stay period is triggered that bars the FDA from authorizing generic entry until 30 months have elapsed or until litigation is resolved, whichever occurs sooner. Generic entry typically occurs between 12.5 and 14.5 years after a branded drug's FDA-approval date. Our study's objective was to measure when stay periods typically expire and how much time remains prior to generic product launch in order to understand the extent to which stay periods could potentially delay the timing of generic entry. FDA, US Food and Drug Administration

tested whether stay periods were associated with shorter or longer timeframes among these four milestone events.

Cohort selection

Based on the findings of previous studies of generic market dynamics that recorded the timing of Paragraph IV certifications and generic launches,[9] we reasoned that 4.6–4.9 years would be required following FDA approvals of the generic drug application (assuming FDA approvals occured 30 months after the Paragraph IV certifications were filed) before observing generic product launch for most drugs. Therefore, we selected an observation window starting with first FDA generic approvals during the years 2013–2015 to the time of study initiation in 2020.

Data extraction

First generic approvals of new molecular entities were identified using the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book")[10] and the Drugs@FDA online database.[11] These data sources contain information on therapeutic equivalence between brand-name and generic products, the approval dates for brand-name and generic products, and copies of the FDA's approval letters. To determine which generic drugs were approved following a Paragraph IV certification, we scoured the FDA's List of Paragraph IV Drug Product Applications and copies of the FDA approval letters.[12] The FDA approval letters from Drugs@FDA were also used to determine whether brand-name companies responded with patent litigation within 45 days after the Paragraph IV certification filing, which was used to create a binary stay variable. Expected stay expirations were calculated according to the specifications in the Hatch-Waxman Act: 30 months after Paragraph IV certification submission date, or 7.5 years after the FDA approval date of the brand-name reference product in question, whichever was later. (The 30-month period begins to run from receipt of notice by the patent owner that a Paragraph IV certification has been made, which notice must be given within 20 days after the

date of the postmark on the notice sent by the FDA to the generic drug manufacturer that its application has been filed, but such notice receipt dates are not readily available.) Finally, to identify generic product launch dates, we performed searches on the generic manufacturers' websites for press releases. Occasionally, there were multiple first generics simultaneously approved by the FDA. We considered each first generic application as a separate unit of analysis, rather than combining it with other applications approved on the same day, as there may be individual variations for the other major events leading to generic entry. Additional detail on our data collection strategy is available in the Supplementary Information.

Analysis

Descriptive statistics are reported on the number of Paragraph IV certifications that led to stay periods. Dates of the key events (i.e., Paragraph IV certification submission date, expected stay expiration, FDA approval of the generic application, and generic product launch) relating to each generic drug were placed along a common timeline by calculating years between their occurrence and the date when their brand-name reference product was FDA-approved. We report our results using medians and interquartile ranges (IQRs) as the data were not normally distributed. To measure the relevance of the 7.5-year provision and its potential impact on the timing of stay expiration, we also calculated the proportion of Paragraph IV certifications that were affected by the 7.5-year provision.

We used the Mann–Whitney–Wilcoxon rank sum test to determine whether the observed differences between drugs with and without stay periods were significantly different (95% confidence level, two-tailed). For drugs with stay periods, we measured the number of years between the expected stay expiration and generic launch. We further noted any cases when generic launch occurred immediately after the expiration of the stay period.

RESULTS

There were 87 first generic approvals of new molecular entities between 2013 and 2015 (Figure 2). Fifty-one (59%)

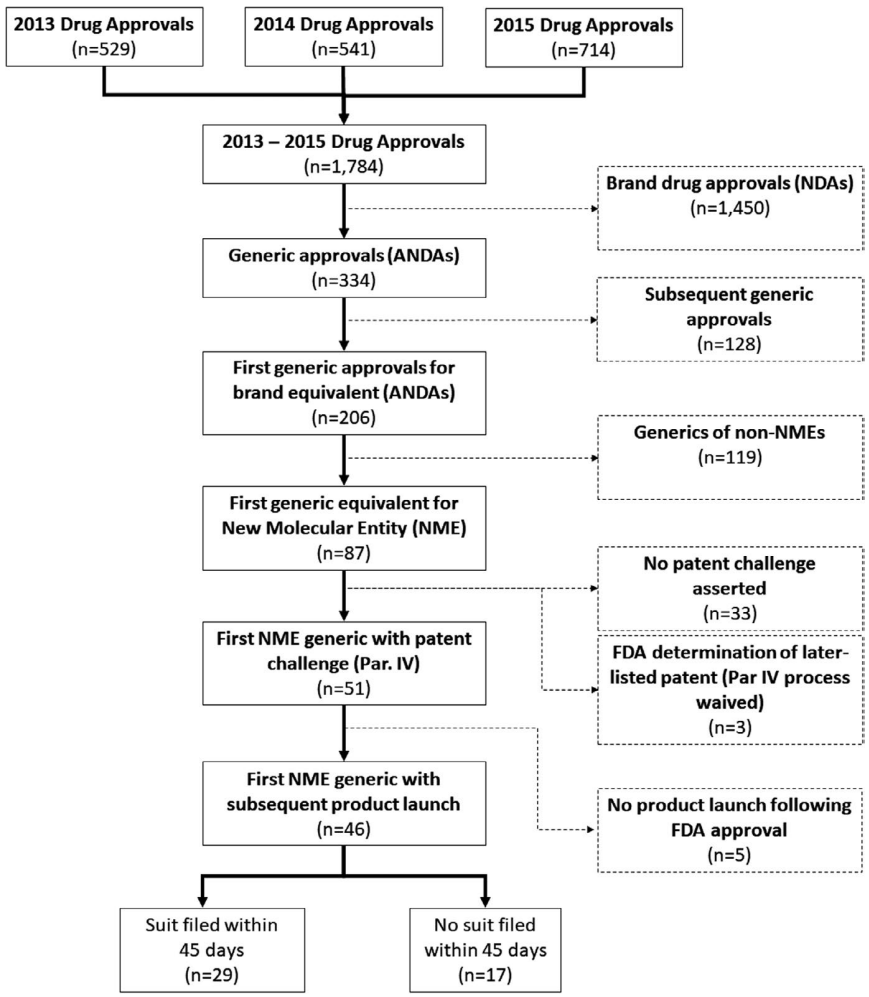


FIGURE 2 Identification of first generic approvals of New Molecular Entities, 2013–2015. ANDAs, abbreviated new drug application; FDA, US Food and Drug Administration; NDAs, new drug application

TABLE 1 Time of and between major milestone events leading to generic entry following submission of a Paragraph IV application

Measure	Overall	Stay period	No stay period	Mann–Whitney–Wilcoxon rank sum test, *p*-value
Number of first generic applications, *n*	46	29	17	—
Timing of milestones leading to generic entry, years (IQR)				
Paragraph IV filing	5.2 (4.0–8.0)	5.2 (4.0–9.2)	5.1 (4.0–7.5)	0.640
Stay expiration	—	7.7 (7.5–10.2)	—	—
FDA approval of Paragraph IV application	11.5 (9.4–14.5)	11.5 (9.4–13.4)	12.2 (9.4–15.0)	0.399
Generic product launch	14.1 (11.1–15.2)	13.7 (11.5–14.5)	14.6 (11.0–15.3)	0.400
Time intervals between milestone events, years (IQR)				
Stay expiration to FDA approval	—	2.1 (0.8–3.1)	—	—
Stay expiration to generic launch	—	3.2 (1.9–6.0)	—	—
Paragraph IV filing to generic launch	7.0 (5.0–8.5)	5.4 (4.4–8.5)	7.2 (6.4–8.1)	0.090

Abbreviations: FDA, US Food and Drug Administration; IQR, interquartile range.

[a]Eleven of these "30-month" stays expired after 7.5 years (i.e., after more than 30 months) because the Paragraph IV application was filed between 4 and 5 years after the approval of the reference brand name product and because brand-name manufacturer filed suit within 45 days.

involved a Paragraph IV certification, and 46 of these launched during our time window, making up our final drug cohort (the remaining 5 were approved but not yet launched by 2020). (These 46 generic products were equivalents to 34 brand-name drugs; the FDA simultaneously approved multiple generic equivalents to 5 brand-name products on the same day.) For 17 (37%) of the 46 drugs in our final cohort, the brand-name manufacturers did not respond with litigation within 45 days of the Paragraph IV certification and a stay period was therefore not triggered. For the remaining 29 drugs (63% of 46), the 30-month stay was triggered.

Timing of milestone events

Paragraph IV certification initiating the litigation process to facilitate generic entry was filed a median of 5.2 years (IQR: 4.0–8.0 years) after the approval of the brand-name drug (Table 1, Figure 3). Of the 46 Paragraph IV certifications, a plurality (14/46, 30%) were filed 4 years after the brand-name reference product was approved. Among the 29 applications with stay periods, the expected expiration of the stay occurred a median of 7.7 years (IQR: 7.5–10.2 years) after the approval of the brand-name drug. Eleven stay periods were extended by the 7.5-year minimum requirement. The FDA approvals of the 46 generic applications occurred a median of 11.5 years (IQR: 9.4–14.5 years) after the brand-name drug approval. Generic product launch occurred a median of 14.1 years (IQR: 11.1–15.2 years) after brand-name drug approval. There were no significant differences in the timing of these milestone events when comparing cases when the stay period was in force ($n = 29$) versus when it was absent ($n = 17$; Table 1).

Timing of generic launches versus stay period expirations

The 29 stay periods expired a median of 3.2 years (IQR: 1.9–6.0 years) prior to generic launch (Table 1). There was one case (nebivolol, a beta-blocker used to treat hypertension) in which generic launch occurred when litigation was resolved via a settlement shortly before its stay period was set to expire (7.5 years after the approval of its brand-name reference product) (Figure 3). Otherwise, no other launches occurred within 1 month of the expected stay expiration, and the next shortest gap in time between expected stay expiration and launch is 10 months.

DISCUSSION

In our review of the milestones leading to generic entry, we found that more than half (59%) of first generic drug approvals were subject to Paragraph IV patent challenges, and that of these challenges, about one-third were initiated by generic manufacturers as soon as permitted by law (4 years after the reference brand drug approval). These challenges resulted in a median expected stay period expiring 7.7 years after approval of the first generic drug product. This means that most new brand-name drugs with litigated patent challenges should expect a minimum of 7.5 years of generic-free market exclusivity, although most will be longer. Nearly all (28/29) stay periods expired several years before the generic launch date, suggesting they did not delay generic entry.

The timing of the milestone events in our cohort is consistent with previous research. For example, a previous study of generic entry found that the time between brand name drug

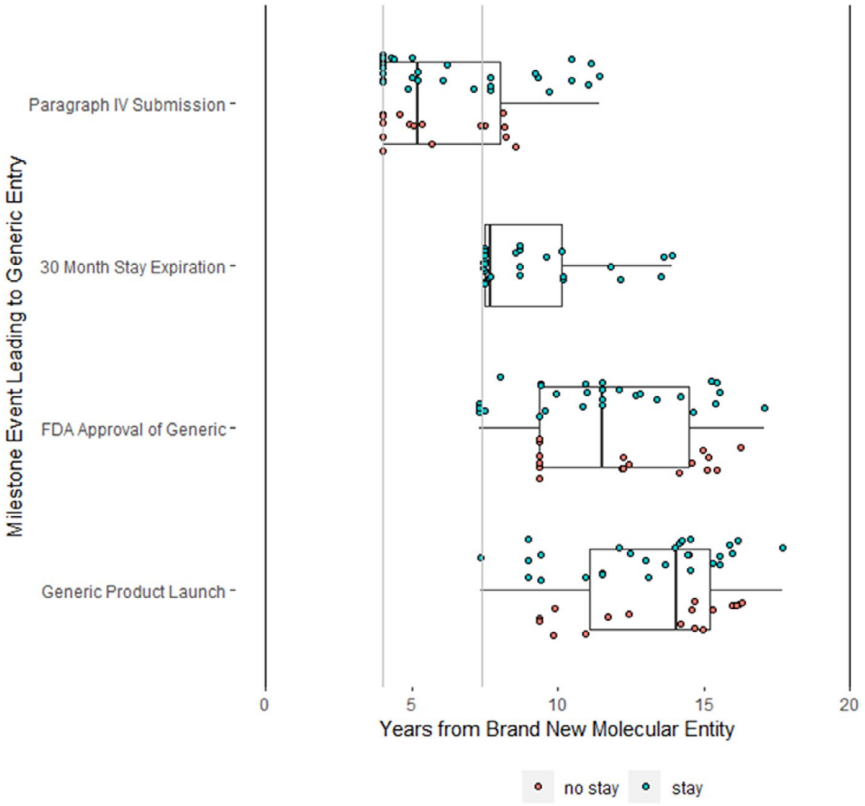


FIGURE 3 Timing of major milestone events leading to generic entry for drugs experiencing Paragraph IV challenges in years since approval of brand equivalent

approval and Paragraph IV certification has been decreasing since 1995, with a 3-year moving average of 6.5 years in 2012 and 5.9 years in 2014, compared to the 5.2-year period described in our study based on a more recent cohort of drugs.[9] This decreasing period suggests intensifying competition in the market for generic drugs, which may in turn reflect a separate Hatch-Waxman incentive that provides the first-filer of a generic drug application with 180-days of exclusivity with respect to other generic drug manufacturers.

Our study also found that generic launch, on average, occurred long after (median 3.2 years) the expected expiration of the 30-month stay period. Possible reasons for this finding include that some patents are found valid, forcing generic drug companies to wait until patent expiration; that some patent litigation is settled, with agreed-upon generic drug entry dates falling between the end of stay periods and patent expiration dates; that patent litigation is ongoing and generic drug manufacturers decline to launch at-risk; and, perhaps most importantly, that the FDA approval of the generic drug application occurred, on average, several years after stay expirations (11.5 vs. 7.7 years after brand-name drug approval).

Our results illustrate some of the advantages of early drug patent dispute resolution. Aside from allowing ample time for court proceedings to reach their natural conclusion so that conflicts over market protections are fully resolved well before generic entry is set to occur, early patent dispute resolution will minimize the amount of time that weak patents later deemed to be invalid or not infringed appear in the Orange Book, create barriers to market entry, and enable high prices, limiting drug accessibility and exerting a public health impact. Early patent dispute resolution provides additional certainty surrounding when future generic entry is likely to occur, which is a benefit for multiple stakeholders including generic manufacturers, practitioners, and patients. Furthermore, earlier filing of applications for generic entry allows more time for FDA review and for generic applicants to respond to requests by the FDA for more information. A policy change that could facilitate earlier patent dispute resolution and earlier FDA review of generic applications would be to remove the 4-year period after brand-name drug approval during which generic drug applications cannot be submitted.

Our study is subject to certain limitations. First, our analysis was based on the 52% (46 of 87) of first generic drugs for which both a Paragraph IV certification was filed and generic launch occurred, and the focus of our calculations was the 33% (29 of 87) of generic drugs for which a 30-month stay was triggered. Assessment of these subsets may not be representative of drugs not subject to certification, stay, or launch. This may help to explain why we found a median period of market time prior to generic entry (14.1 years) that was on the high end of the range described in previous studies not limited to drugs subject to Paragraph IV certification (12–14.5 years).[9,13–17] Second, our study examined only new molecular entities. As generic entry tends to occur sooner for modified versions of existing drugs (e.g., after about 8.25 years[13,16]), litigation could play a different role in the timing of generic entry for

such drugs. Third, our study did not consider the possibility that courts can shorten or prolong stay periods if either litigant fails to reasonably cooperate in expediting the proceedings, nor did we attempt to measure how frequently this occurs.[3] Finally, whereas our study found that generic manufacturers often (30% of first generic drugs) began the patent challenge process as soon as legally permitted, the study's focus upon marketed products did not consider the possibility that stay periods could discourage generic applicants from initiating or continuing with the Paragraph IV process.

CONCLUSION

When 30-month stay periods are triggered, which occurred for 29 (33%) of 87 first generics in our study, they nearly always (28 of 29) expire well before generic entry occurs. Nevertheless, stays can be important if they delay generic entry for high-cost or high-volume brand-name drugs. Early patent resolution has several advantages, including that stay periods are unlikely to directly impact the timing of generic entry and that questionable patent claims can be tested before patentees accrue additional time on an exclusive market (a right reserved for true innovations). One way to facilitate earlier patent dispute resolution is to remove the stipulation that generic drug applications can be submitted only after 4 years have elapsed from the brand-name drug's FDA approval date.

CONFLICT OF INTEREST

The authors declared no competing interests for this work.

AUTHOR CONTRIBUTIONS

S.K., J.J.D., A.S.K., and R.F.B. wrote the manuscript. S.K., J.J.D., A.S.K., and R.F.B. designed the research. S.K. and R.F.B. performed the research. S.K., J.J.D., A.S.K., and R.F.B. analyzed the data. S.K. and R.F.B. contributed new analytical tools.

REFERENCES

1. 21 U.S.C. § 355.
2. Melling P, Khabarov D, Trusov A, Ermolina D. Global guide to patent linkage. Baker McKenzie. 2019. https://www.bakermckenzie.com/en/insight/publications/guides/global-guide-to-patent-linkage. Accessed February 1, 2021.
3. Lewis J, Ikahihifo-Bender N. When courts allow changes to Hatch-Waxman 30-Month Stay. Law360. 2018. https://www.law360.com/articles/1080769/when-courts-allow-changes-to-hatch-waxman-30-month-stay. Accessed February 1, 2021.
4. Schacht WH, Thomas JR, Resources S, Division I. *The Hatch-Waxman Act: proposed legislative changes affecting pharmaceutical patents*. Washington, DC: Congressional Research Service; 2003.
5. Hui YF. FDA's proposed rules on patent listing requirements for new drug and 30-month stays on ANDA approval (Proposed Oct. 24, 2002). *Ann Health Law*. 2003;12:325.
6. Young AK, Andrus MS. Pharmaceutical pricing and Hatch-Waxman reform: the right prescription. *J Generic Med*. 2004;1(3):228-237.
7. Bhat VN. Patent term extension strategies in the pharmaceutical industry. *Pharm Policy Law*. 2005;6:109-122.
8. Wirz M. Are patents really limited to 20 years: a closer look at pharmaceuticals. *Okla JL & Tech*. 2003;1:1.
9. Grabowski HG, Long G, Mortimer R, Boyo A. Updated trends in US brand-name and generic drug competition. *J Med Econ*. 2016;19(9):836-844.
10. United States Food and Drug Administration. *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*. United States Food and Drug Administration. http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Published 2021. Accessed February 1, 2021.
11. United States Food and Drug Administration. Drugs@FDA: FDA approved drug products. United States Food and Drug Administration. https://www.accessdata.fda.gov/scripts/cder/daf/. Published 2021. Accessed February 1, 2021.
12. United States Food and Drug Administration. Paragraph IV patent certifications. United States Food and Drug Administration. 2021. https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/abbreviatednewdrugapplicationandagenerics/ucm047676.htm. Accessed February 1, 2021.
13. Beall RF, Darrow JJ, Kesselheim AS. A method for approximating future entry of generic drugs. *Value Health*. 2018;21(12):1382-1389.
14. Grabowski HG, Kyle M. Generic competition and market exclusivity periods in pharmaceuticals. *MDE Manage Decis Econ*. 2007;28(4–5):491-502.
15. Grabowski HG, Vernon JM. Effective patent life in pharmaceuticals. *Int J Technol*. 2000;19(1–2):98-120.
16. Hemphill CS, Sampat BN. Evergreening, patent challenges, and effective market life in pharmaceuticals. *Health Econ*. 2012;31(2):327-339.
17. Wang B, Liu J, Kesselheim AS. Variations in time of market exclusivity among top-selling prescription drugs in the United States. *JAMA Intern Med*. 2015;175(4):635-637.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Kannappan S, Darrow JJ, Kesselheim AS, Beall RF. The timing of 30-month stay expirations and generic entry: A cohort study of first generics, 2013–2020. *Clin Transl Sci*. 2021;14:1917–1923. https://doi.org/10.1111/cts.13046

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC., NORTON (WATERFORD) LTD., and TEVA PHARMACEUTICALS USA, INC., Plaintiffs, v. AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL IRELAND LIMITED, AMNEAL PHARMACEUTICALS LLC, and AMNEAL PHARMACEUTICALS INC., Defendants.	Civil Action No. 23-cv-20964-SRC-MAH **NOTICE OF APPEAL** *Filed Electronically*

NOTICE IS HEREBY GIVEN that Plaintiffs Teva Branded Pharmaceutical Products R&D, Inc., Norton (Waterford) Ltd., and Teva Pharmaceuticals USA, Inc. (collectively, "Teva" or "Plaintiffs") hereby appeal to the United States Court of Appeals for the Federal Circuit pursuant to Federal Rule of Appellate Procedure 3 and 28 U.S.C. § 1295 from the Court's Order and Opinion entered on June 10, 2024 granting an injunction (D.E. 88), as well as any and all other judgments, orders, opinions, rulings, and findings that merge therein or are pertinent or ancillary to the foregoing that are adverse to Plaintiffs.

Payment of the required $605 fee is provided with this Notice of Appeal. This fee includes the $600 fee for docketing a case on appeal required by 28 U.S.C. § 1913 and Federal Circuit Rule 52(a)(2), and the $5 fee for filing a notice of appeal required by 28 U.S.C. § 1917.

Dated: June 11, 2024

OF COUNSEL:

Daryl L. Wiesen
(DWiesen@goodwinlaw.com)
Christopher T. Holding
(CHolding@goodwinlaw.com)
Louis L. Lobel
(LLobel@goodwinlaw.com)
Thomas V. McTigue IV
(TMcTigue@goodwinlaw.com)
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
(617) 570-1000

Natasha E. Daughtrey
(NDaughtrey@goodwinlaw.com)
GOODWIN PROCTER LLP
601 South Figueroa Street
Los Angeles, CA 90017
(213) 426-2642

Kathryn S. Kayali
(kkayali@wc.com)
WILLIAMS & CONNOLLY LLP
680 Maine Avenue, S.W.
Washington, DC 20024
(202) 434-5000

/s/ Liza M. Walsh
Liza M. Walsh (lwalsh@walsh.law)
Selina M. Ellis (sellis@walsh.law)
Hector D. Ruiz (hruiz@walsh.law)
Christine P. Clark (cclark@walsh.law)
WALSH PIZZI O'REILLY FALANGA LLP
Three Gateway Center
100 Mulberry Street, 15th Floor
Newark, New Jersey 07102
Tel: (973) 757-1100

Attorneys for Plaintiffs Teva Branded Pharmaceutical Products R&D, Inc., Norton (Waterford) Ltd., and Teva Pharmaceuticals USA, Inc.

present it to the Federal Circuit court of appeals.

There is no harm to Amneal because they can't conceivably go on the market.

And the public interest, as you have conceded, is not harmed in any way, shape, or form by granting that stay.

Now I can also tell you, quite candidly, just like I indicated that the Federal Circuit and the district courts do not appreciate being presented with urgent applications without adequate time to consider them. Your proposal that we proceed to a preliminary injunction on this instead, quite frankly, is one which is indeed anathema to the undersigned, meaning me. All right.

There is nothing worse than having to deal with complex legal and factual issues on an expedited basis because a generic has gone on the market at risk and a branded manufacturer, therefore, is compelled to seek a preliminary injunction. It creates havoc with the court's docket and it delays handling other cases. And the court is satisfied that granting that stay will obviate that possibility.

So for the reasons that I just discussed, the alternate application by Teva for this matter to be stayed for a period of 30 days from today is granted. I will direct Teva to submit a form of order.

I am also going to direct you folks to consult and agree upon a briefing schedule for any such application, which

B. Disputed Constructions

Pursuant to Local Patent Rule 4.3(b), attached hereto as Exhibit A is a claim chart identifying the claim terms in dispute, the parties' proposed constructions, and the evidence (both intrinsic and extrinsic) that each party intends to rely on in support of its proposed construction or to oppose the other party's proposed construction. Included in the below table is a summary of the disputed claim terms, their corresponding asserted claim numbers, and the parties' proposed constructions. The parties will supplement this JCCS if they are able to reach agreement on any additional terms.

No.	Claim Term Patent(s) / Claim(s)	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
1	"An inhaler for metered dose inhalation" '289 patent, claim 1 '587 patent, claims 1, 12	The preamble is limiting. Plain and ordinary meaning in view of the claims, specification, and prosecution history, which is: "An inhaler for metered dose inhalation containing an active drug capable of being dispensed via the inhaler to the lungs"	The phrase "An inhaler for metered dose inhalation" is part of the preamble and is not limiting. Therefore, no construction is necessary. To the extent the Court finds that this phrase is limiting and requires construction, this phrase should be construed as "An inhaler device for metered dose inhalation"
2	"medicament canister" '289 patent, claims 1, 2 '587 patent, claims 1, 2, 12	Plain and ordinary meaning in view of the claims, specification, and prosecution history, which is: "a canister containing an active drug capable of being dispensed via the inhaler to the lungs"	No construction necessary. Plain and ordinary meaning, i.e., "a canister for medicament"
3	"A dose counter for an inhaler"	The preamble is limiting. Plain and ordinary meaning in view of the claims,	The phrase "A dose counter for an inhaler" is part of the preamble and is not limiting.

No.	Claim Term Patent(s) / Claim(s)	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
	'808 patent, claim 1	specification, and prosecution history, which is: "A dose counter used in connection with an inhaler"	Therefore, no construction is necessary. To the extent the Court finds that this phrase is limiting and requires construction, this phrase should be construed as "A dose counter for an inhaler device"
4	"an inhaler" '808 patent, claim 1	The preamble is limiting. Plain and ordinary meaning in view of the claims, specification, and prosecution history, which is: "an inhaler containing an active drug capable of being dispensed via the inhaler to the lungs"	The phrase "an inhaler" is part of the preamble and is not limiting. Therefore, no construction is necessary. To the extent the Court finds that this phrase is limiting and requires construction, this phrase should be construed as "an inhaler device"
5	"An incremental dose counter for a metered dose inhaler" '889 patent, claim 1	The preamble is limiting. Plain and ordinary meaning in view of the claims, specification, and prosecution history, which is: "An incremental dose counter used in connection with a metered dose inhaler"	The phrase "An incremental dose counter for a metered dose inhaler" is part of the preamble and is not limiting. Therefore, no construction is necessary. To the extent the Court finds that this phrase is limiting and requires construction, this phrase should be construed as "An incremental dose counter for a metered dose inhaler device"
6	"a metered dose inhaler" '889 patent, claim 1	The preamble is limiting. Plain and ordinary meaning in view of the claims, specification, and prosecution history, which is:	The phrase "a metered dose inhaler" is part of the preamble and is not limiting. Therefore, no construction is necessary.

No.	Claim Term Patent(s) / Claim(s)	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
		"a metered dose inhaler containing an active drug capable of being dispensed via the inhaler to the lungs"	To the extent the Court finds that this phrase is limiting and requires construction, this phrase should be construed as "a metered dose inhaler device"
7	"canister" '889 patent, claim 1	Plain and ordinary meaning in view of the claims, specification, and prosecution history, which is: "a canister containing an active drug capable of being dispensed via the inhaler to the lungs"	No construction necessary. Plain and ordinary meaning, i.e., "canister"

C. Claim Terms Whose Construction Will Be Most Significant to the Resolution of the Case

Pursuant to Local Patent Rule 4.3(c), the parties do not believe that the construction of any of the disputed terms will be case dispositive or substantially conducive to promoting settlement.

D. Anticipated Length of Time Necessary for the Claim Construction Hearing

Pursuant to Local Patent Rule 4.3(d), the parties anticipate and respectfully request four hours, split evenly between the sides, for the Claim Construction Hearing. To the extent the Court allocates a different amount of time for the hearing, the parties respectfully request that the allocated time be split evenly between the sides.

E. Identification of Witnesses for the Claim Construction Hearing

Pursuant to Local Patent Rule 4.3(e), the parties do not intend to call any witnesses at the Claim Construction Hearing.