Minute Order Form (06/97)

United States District Court, Northern District of Illinois

Name of Assigned Judge or Magistrate Judge	Richard Posner	Sitting Judge if Other than Assigned Judge	
CASE NUMBER	98 C 3952	DATE	3/3/2003
CASE TITLE	SmithKline Beecham et al vs. Apotex Corp. et al		

[In the following box (a) indicate the party filing the motion, e.g., plaintiff, defendant, 3rd party plaintiff, and (b) state briefly the nature of the motion being presented.]

MOTION:

DOCKET ENTRY:

(1) ☐ Filed motion of [use listing in "Motion" box above.]

(2) ☐ Brief in support of motion due _____.

(3) ☐ Answer brief to motion due_____. Reply to answer brief due_____.

(4) ☐ Ruling/Hearing on _____ set for _____ at _____.

(5) ☐ Status hearing[held/continued to] [set for/re-set for] on _____ set for _____ at _____.

(6) ☐ Pretrial conference[held/continued to] [set for/re-set for] on _____ set for _____ at _____.

(7) ☐ Trial[set for/re-set for] on _____ at _____.

(8) ☐ [Bench/Jury trial] [Hearing] held/continued to _____ at _____.

(9) ☐ This case is dismissed [with/without] prejudice and without costs[by/agreement/pursuant to]
☐ FRCP4(m) ☐ Local Rule 41.1 ☐ FRCP41(a)(1) ☐ FRCP41(a)(2).

(10) ■ [Other docket entry] **ENTER OPINION:** The Court hereby finds in favor of the defendants (the Apotex parties) and against the plaintiffs (the SmithKline parties), and the suit is dismissed with prejudice. All pending motions are denied as moot.

(11) ■ [For further detail see order attached to the original minute order.]

	No notices required, advised in open court.		number of notices	Document Number
	No notices required.			
	Notices mailed by judge's staff.		MAR 03 2003 date docketed	
	Notified counsel by telephone.			
✓	Docketing to mail notices.		docketing deputy initials	351
✓	Mail AO 450 form.			
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IN THE
UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF
ILLINOIS, EASTERN DIVISION

SMITHKLINE BEECHAM CORP. and BEECHAM GROUP, P.L.C.,	)	
Plaintiffs,	)	No. 98 C 3952
v.	)	**Richard A. Posner,** *Circuit Judge.*
APOTEX CORP., APOTEX, INC., and TORPHARM, INC.,	)	
Defendants.	)	

OPINION

I conducted a bench trial in this patent infringement case between February 5 and 21 of this year, by designation of the chief circuit judge pursuant to 28 U.S.C. § 291(b), and this opinion comprises the findings of fact and conclusions of law that Fed. R. Civ. P. 52(a) requires me to issue. The plaintiffs in their post-trial brief erroneously refer to "findings" that I made in the course of the trial. I made no findings during the trial; these are my findings.

The Procedural Setting and Pretrial Rulings

The plaintiffs are two subsidiaries of Glaxo, the British manufacturer of pharmaceutical drugs. I shall refer to the two collectively as SmithKline. The defendants are Apotex, Inc., a Canadian manufacturer of generic pharmaceuticals, and affili-

ates of it; I shall refer to the defendants collectively as "Apotex." SmithKline claims that Apotex is (more precisely, as I'll explain in due course, will be) infringing SmithKline's U.S. patent 4,721,723, or "723" as the parties refer to it, after its last three digits. The patent is on an antidepressant drug that SmithKline sells under the trade name Paxil. Paxil is now the leading brand of antidepressant drug, with annual sales of $3.2 billion worldwide, about two-thirds in the United States.

SmithKline argues not only that Apotex is an infringer but also that the infringement is willful, entitling SmithKline to additional relief, namely an award of attorneys' fees. Apotex contends that the patent (more precisely, the claim in the patent that covers the composition of the drug, as distinct from claims concerning processes for making the drug) is invalid but, if valid, not infringed, and if valid and infringed still not infringed willfully. I deferred consideration of the issue of willfulness to such time as I might hold the patent valid and infringed. Since I hold that the patent although valid is not infringed and further that even if it is valid and infringed SmithKline is entitled to no relief, I do not reach the issue of willfulness. Should the case be remanded to me, I would have to conduct a further evidentiary hearing in order to resolve that issue.

Judge (now Chief Judge) Kocoras of the Northern District of Illinois, to whom the case was initially assigned when it was filed back in 1998, made a number of pretrial rulings, and I must consider the extent to which I am bound by them in accordance with the doctrine of law of the case. The doctrine requires a court to adhere to its previous rulings in the same litigation unless there is a compelling reason, such as an intervening change of law or newly discovered evidence, to reexamine them. Its usual application is to a case that is remanded by the court of appeals and then returns to that court by an appeal from the decision on remand. The doctrine counsels the court not to revisit the issues it decided on the first appeal, but it does not limit a trial judge's changes of mind during the course of a litigation uninterrupted by an appeal, and such changes of mind are of course frequent. When however the judges in a

case are switched in midstream, as happened here, the successor judge may not reconsider his predecessor's rulings with the same freedom that he may reconsider his own rulings. "As this court [the Seventh Circuit] explained in *Williams v. C.I.R.*, 1 F.3d 502 (7th Cir. 1993), the law of the case doctrine in these circumstances reflects the rightful expectation of litigants that a change of judges mid-way through a case will not mean going back to square one. See also *Christianson v. Colt Industries Operating Corp.*, 486 U.S. 800, 816–17 (1988). Although the second judge may alter previous rulings if he is convinced they are incorrect, 'he is not free to do so...merely because he has a different view of the law or facts from the first judge.' *Williams*, 1 F.3d at 503. Instead, the presumption is that earlier rulings will stand, even though it can be overcome for compelling reasons (such as new controlling law or clear error)." *Best v. Shell Oil Co.*, 107 F.3d 544, 546 (7th Cir. 1997); see also *Peterson v. Lindner*, 765 F.2d 698, 704 (7th Cir. 1985); *Fagan v. City of Vineland*, 22 F.3d 1283, 1290 (3d Cir. 1994).

The reader may wonder at my citing Seventh Circuit rather than Federal Circuit cases on this point, since if my decision is appealed it will be appealed to the Federal Circuit. But that court applies the law of the circuit in which the district court is located to procedural matters that are not unique either to patent law or to appellate as distinct from trial procedure. See *Panduit Corp. v. All States Plastic Mfg. Co.*, 744 F.2d 1564, 1574–75 (Fed. Cir. 1984) (per curiam); *Biodex Corp. v. Loredan Biomedical, Inc.*, 946 F.2d 850, 858 (Fed. Cir. 1991). The doctrine of law of the case is not unique in either sense and so its application here is governed by Seventh Circuit (and of course Supreme Court) precedent.

The parties asked me to reexamine several of Judge Kocoras's rulings, but only one met the criteria for reexamination, his order of July 16, 2002. That order excluded evidence that infringement of SmithKline's patent 723 would occur when Apotex's product combined with the fluids in a patient's stomach to create small amounts of the patented product, or perhaps even earlier when the patient opened the bottle of tablets and took out a pill, reexposing it as well as the remaining pills

in the bottle to air and hence to moisture. The patient would be the infringer in either of those cases (assuming that there is any infringer in those cases, which I express no view on), but SmithKline argues that Apotex, knowing that infringement would occur, would be guilty of inducement to infringe. 35 U.S.C. § 271(b). As it pointed out in its motion to vacate the July 16 order, the Federal Circuit's decision in *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed. Cir. 2003), undercuts the ground of that order and so reexamination is warranted. But *Warner-Lambert* also makes clear that the burden of proving inducement is a heavy one, *id.* at 1363–64, and SmithKline's motion provided no ground for thinking that SmithKline could carry the burden. Even if a patient's gastrointestinal juices convert the nonpatented product that Apotex plans to manufacture to the product patented by SmithKline and Apotex knows this will happen, there is no evidence that Apotex intends, in the sense of desires or is working to achieve, this result. For the gastrointestinal "infringement" does nothing for Apotex commercially; it merely increases Apotex's exposure to liability. That is equally true if infringement is thought to occur when the bottle is opened. Apotex has tried to prevent conversion of its product to the patented form and a principal issue in this case is whether it has succeeded; there is no suggestion that Apotex *desires* conversion. I therefore denied the motion to vacate the July 16 order and I adhere to that ruling. But I add that, in light of the discussion of relief in the last part of this opinion, it is plain that if SmithKline were guilty of inducement in the circumstances outlined above, it would not be entitled to any relief.

The Background of the Case

Early in 1977 a British company called Ferrosan obtained a U.S. patent ("196," also known as the Christensen patent) on a set of compounds that included what came to be called "paroxetine." The paroxetine molecule consists of carbon, nitrogen, oxygen, hydrogen, and fluorine atoms arranged in a particular configuration. When combined with additional atoms to form a salt molecule (a hydrochloride, for example, if paroxetine base

is bathed in hydrochloric acid), and mixed with additional compounds (binders, lubricants, disintegrants, etc.—collectively, "excipients") to bulk up into a pill and to improve handling, tableting, and dissolution, paroxetine was believed, correctly as it turned out, to be effective in treating depression and related psychiatric disorders. Like fluoxetine—the active ingredient in Prozac—paroxetine is a selective serotonin reuptake inhibitor, which helps to assure an adequate supply of the "feel good" enzyme serotinin to brain cells. Although mention of Prozac is a reminder that Paxil faces competition from other SSRIs (not to mention other types of antidepressant drug and other modes of treatment altogether), there are medically significant differences, both in efficacy and side effects, even among the different SSRIs. Paxil, for example, is preferred to Prozac by many doctors for the treatment of depression coupled with anxiety (a common combination), because unlike Prozac it has been approved by the Food and Drug Administration for anxiety disorders.

Ferrosan was not a manufacturer of pharmaceutical drugs, so in 1980 it licensed its paroxetine patent to SmithKline. Although the patent specified paroxetine maleate as the paroxetine salt it was claiming, Ferrosan had already, after some travail, succeeded in creating a paroxetine hydrochloride in crystalline form, hydrochloride being a preferred salt for pharmaceutical purposes. In 1981 SmithKline began manufacturing paroxetine hydrochloride in its Harlow (U.K.) plant.

Before a pharmaceutical drug can be placed on the market, it must undergo elaborate testing for safety and efficacy, and so quantities of paroxetine hydrochloride were distributed to different parts of the world, including the United States, for use in clinical trials. SmithKline has a laboratory in Worthing, England, and samples of paroxetine hydrochloride were sent there in bulk form—that is, before being made into pills—to be used in experiments on improving the production of the bulk material. In March 1985, a chemist at Worthing, Alan Curzons, experimenting on ways to produce paroxetine hydrochloride, discovered that he had created a new form of the compound, which he dubbed "Form 1" to distinguish it from the anhydrous

form, which he dubbed (confusingly, because it was the earlier form) Form 2. Tests that Curzons performed confirmed that Form 1 was indeed a distinct crystalline form of paroxetine hydrochloride.

Crystallinity is central to this case. When molecules are bound together, by interatomic forces that radiate beyond the "boundaries" of the molecules themselves, in a definite structure which is then repeated over and over again without significant change, the agglomerations that result are called "crystals." (These and other relevant aspects of crystallography are lucidly discussed in Stephen R. Byrn, Ralph R. Pfeiffer & Joseph G. Stowell, *Solid-State Chemistry of Drugs* (2d ed. 1999). See especially Chapters 1, 10–11, and 13. Dr. Byrn testified for SmithKline at the trial.) The molecules are like the intersections of the slats of a lattice; the slats correspond to the forces that hold the molecules in their fixed positions, and the multiplication of the lattice is the crystal. The crystal's minimum structure—the structure that, repeated, constitutes the crystal—is called the "unit crystal cell." The unit crystal cell is not itself a crystal, however. That is by definition: a crystal is a multiple of the structure that defines the unit crystal cell. Moreover, were there only, say, two unit crystal cells, the molecules composing them would not crystallize because the interatomic forces would be too weak to maintain the structure. The number of unit crystal cells required to create the minimum crystal is very small, however: depending on the molecules and the structure, as few as ten molecules may be enough to create an actual crystal. Stated differently, a large crystal might in principle though not in practice be cut into an immense number of utterly minute crystals.

The same substance will sometimes appear in more than one crystalline form—will be, that is, "polymorphous." The molecules are the same but the lattice is different. The difference can affect the melting point of the crystal (the point at which the crystal structure is destroyed by heat, rendering the substance liquid) and other properties of the crystal, such as hardness: a dramatic example is graphite and diamonds, both of which are crystals of carbon. Because a different arrange-

ment of molecules implies a different pattern of bonds, and different bonds vibrate at different frequencies, different polymorphs of the same chemical produce different x-ray diffraction patterns and infrared spectra, which are two types of graphic mapping of the atomic forces binding the crystal.

The form of paroxetine hydrochloride that Curzons discovered was not a true polymorph, although often and loosely referred to as such, as I shall do; rather, it was a "pseudopolymorph." These critters not only have their molecules arranged differently but also have a slightly different molecular composition. A common type of pseudopolymorph is a *solvate*, which is a crystal in which molecules of a solvent, such as water, have become "caught" inside the crystal and have bonded with the other molecules in an altered crystalline structure. When the trapped and bonded solvent is water, the solvate is called a *hydrate*. And when it is a hydrate in which there is one water molecule for every two of the other molecules constituting the unit crystal cell, in this case molecules of paroxetine hydrochloride, the hydrate is called a *hemihydrate*. Despite the presence of water molecules, a hemihydrate is a solid, a powder, at room temperature.

At the time that Curzons had his eureka moment, SmithKline's plant at Harlow was producing only a paroxetine hydrochloride anhydrate (at least as far as it knew), which is to say a crystalline form of paroxetine that does not contain a bound water molecule. (This anhydrate is what Curzons dubbed "Form 2.") Curzons made a batch of paroxetine, added isopropyl alcohol, a solvent, and found that the batch crystallized as a hemihydrate rather than as an anhydrate. And here an oddity, as it strikes a lay observer at any rate, should be noted. The anhydrous form of crystalline paroxetine hydrochloride is hygroscopic; that is, it attracts water, perhaps because of the position of the fluorine atoms in the anhydrous form, though this was merely a speculation by one of the expert witnesses. The water it attracts either sits on the outside of the paroxetine molecule, loosely attached and therefore easily dispersed by heating at a significantly lower temperature than required to liberate the bound water molecule from the hemi-

hydrate, or, if it has found its way inside the crystal, it is nevertheless again readily dispersed, because it is not held to the paroxetine molecules by strong interatomic bonds. In contrast, the hemihydrate is not hygroscopic because it is not "thirsty"—it has already drunk, as it were.

The anhydrate's hygroscopicity makes it difficult to handle in the manufacturing process; measures must be taken to control humidity and other sources of moisture lest the anhydrate become so "soggy" that it degrades into other compounds, which might impair the safety or efficacy of the product. So when Curzons realized that he had obtained a hemihydrate he immediately grasped the potential commercial significance—and also and distinctly the potential *patent* significance, which has now to be explained—of his discovery.

Because it takes a long time for a new drug to be approved by the U.S. Food and Drug Administration for sale to the American public, the actual period during which the producer has an exclusive right to make, use, and sell the drug is shorter than the statutory term of the patent. In the case of patent 723 for example, the patent at issue in this case, the application was filed in 1985 and granted in 1988, and the patent expires in 2006; but because the FDA process delayed the commencement of commercial sale to 1993 (FDA approval having been obtained the previous year), the effective term of the patent has been compressed to 13 years. Indeed, were it not for 35 U.S.C. § 156(c), a provision added to the patent statute by the Hatch-Waxman Act (the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98–417, 98 Stat. 1585 (1984)), SmithKline would have had only 12 years of effective patent protection, because, were it not for that provision, patent 723 would expire in 2005—20 years after the date of application and 17 years after the date the patent was issued—rather than in 2006.

The compression of the commercially significant patent term by reason of the regulatory process at the FDA is a matter of concern to the manufacturers of new drugs. The cost of developing such a drug is often very great, in part because attempts to develop a new drug that will be both safe and effec-

tive often fail and the cost of these "dry holes" must be reckoned into the cost of the drugs that succeed, as it is only out of the revenues of those drugs that the costs of the dry holes can be recovered. The greater the upfront cost of developing a product, the more time is required to recoup the cost and so (other things being equal) the longer is the socially optimal patent term. The costs incurred in running the gauntlet of FDA approval not only increase the manufacturer's upfront development cost but compound the effect of the delay, also due largely to the FDA, between obtaining a patent and actually being able to market the patented drug to the consuming public. Although Ferrosan obtained its patent on paroxetine in 1977, the product still had not come to market as of 1985, when it was superseded in SmithKline's patent planning by the hemihydrate discovered that year.

Until the Hatch-Waxman Act was passed in 1984, the costs and delays imposed by the FDA's procedures worked in favor of as well as against the manufacturers of patentable drugs. The reason is that generic manufacturers (such as Apotex), that is, manufacturers of drugs that have come off patent, either because the patent has been invalidated or, more commonly, because the patent has expired, also have to obtain the FDA's approval before they can sell the generic drug in the United States. And, before Hatch-Waxman, the generic manufacturer could not, in demonstrating to the FDA that his generic version would be no less safe and effective than the patented original, rely on the animal and human tests conducted by the manufacturer of the patented drug. He had to do his own tests. This required him to make or use the patented product, but he could not do so lawfully before the drug came off patent unless he had a license from the patentee—otherwise he would be an infringer because the Federal Circuit had held that the "experimental use" defense to patent infringement was inapplicable to experiments having commercial aims. *Roche Products, Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858, 863 (Fed. Cir. 1984). The upshot was that the generic manufacturer could not begin the process of seeking FDA approval until the patent expired, and given the length of that process the practical effect was to

extend the period of patent protection well beyond the statutory term. The Hatch-Waxman Act shortened the process both by allowing the generic companies to take a free ride on the results of the patentee's safety and efficacy testing so long as they could show that their product was bioequivalent to the original and by allowing them to make and use the patented product, even though the patent hadn't yet expired, in order to demonstrate bioequivalence.

This case differs from the standard case to which Hatch-Waxman applies because Apotex claims to be making a drug that while bioequivalent to a patented drug does not infringe the patent because it is a different compound. Apotex still had to convince the FDA of this bioequivalence, and whether to aid in demonstrating this or (more likely) merely to learn more about the production of paroxetine, Apotex bought some Paxil tablets, extracted the hemihydrate from them, and even made its own hemihydrate. Although this experimentation amounted to a making or use (in fact both) of the patented hemihydrate, SmithKline concedes that it was not infringement because it fell within the expanded experimental-use privilege created by the Hatch-Waxman Act.

The Act allows the generic manufacturer to file an Abbreviated New Drug Application (ANDA)—abbreviated because the applicant has only to demonstrate bioequivalence, and not safety and efficacy as an original matter—*before* the patent expires on the drug that it wants to produce and sell, though it may not begin to sell the drug until the patent either expires or is declared invalid. If the manufacturer wants to sell its generic equivalent before expiration of the patent, on the ground that the patent either is invalid or won't be infringed because while the two drugs are bioequivalent they are not the same invention, he has to so state in his ANDA. The Act authorizes the patentee in such a case, if he doesn't agree that the patent is invalid or even if valid will not be infringed, to sue the generic manufacturer for infringement, even though there is no infringement in the usual sense because the generic manufacturer has not yet begun to make (other than for permitted experimental purposes) or sell his knock-off of the patented drug.

Had the Act stopped there, its unequivocal effect would have been to shorten the economically significant patent term of drugs. But as a concession to the manufacturers of patented drugs, who had complained with much support in the academic literature about the length of time it took to get a new drug approved by the FDA, Congress tolled the date of expiration of drug patents (the patent term for all utility patents, including therefore drug patents, was then 17 years but in 1995 it was increased to 20 years) during the period in which an application for a new drug was under regulatory review. The Act capped the extension for patents such as 723 issued after the Act was passed at five years. 35 U.S.C. § 156(g)(6)(A). And patent protection could not extend beyond 14 years after the FDA had approved the new-drug application. 35 U.S.C. § 156(c)(3).

The manufacturers of patented drugs were not happy about the trade, in part at least for a reason that the facts of the present case illuminate. The Ferrosan patent (patent 196) expired in 1992. Yet as I have pointed out, as late as 1984, with only eight years to expiration, paroxetine made under that patent had not yet been placed on the market. If, however, the hemihydrate version of the molecule could be patented, the effect might be a considerable extension in the effective patent term of paroxetine because it might become difficult or even impossible to manufacture the pure anhydrous form after the Ferrosan patent expired.

How so? Dr. Joel Bernstein, one of SmithKline's expert witnesses at the trial, is an authority on "disappearing polymorphs." See Joel Bernstein, *Polymorphism in Molecular Crystals* 89–92 (2002); J.D. Dunitz & J. Bernstein, "Disappearing Polymorphs," 28 *Accounts of Chem. Res.* 193 (1995); see also Byrn, Pfeiffer & Stowell, *supra*, at 463. The term refers to the fact that after a new polymorph or pseudopolymorph appears, the process that had been used to make the old polymorph may no longer produce it—may produce instead the new one. Actually there's an ambiguity buried in this formulation that is important to this case. A polymorph could disappear in the literal sense that it could no longer be created; or it could disappear in the more limited sense that the *pure* form of the old polymorph

could no longer be created—the new polymorph would be an indelible though possibly minor and functionally inert component of any batch of the old.

The causal mechanism of polymorphic creation and transformation is not clear—polymorphism simply is not well understood by science, because of the complexity of the atomic interactions that produce it—but it seems to involve the confluence of three factors. First, according to Ostwald's Rule, a well-attested scientific principle, later-appearing polymorphs tend to be more stable than the earlier ones. If there is metamorphosis (interconversion, chemists call it), it tends naturally to be in the direction of more stable forms. A more stable form is less likely to change into a less stable one than vice versa, and so there is a drift toward the more stable polymorphs.

Second, impurities retard crystallization, including crystallization in new forms, and the progress of technology has yielded a secular decline in the proportion of impurities in manufactured products. And third, once a new and more stable crystal emerges, should it be mixed, even in very small quantities, with the old, less stable crystal, the old form may convert to the new. This process of "seeding" the old with the new can be deliberate—that is, can be a method of manufacturing the new polymorph—or adventitious, a result of the fact that some of the crystals become airborne and "contaminate" the laboratory or plant in which the old crystal is being manufactured.

I must pause over the terms "seed" and "seeding" because of the importance they assumed in the trial. In its broadest crystallographic sense a seed is any bit of matter that precipitates crystallization; it could be a grain of dust. But the seeds relevant to this case are seeds that cause one polymorph to convert to another and these seeds are crystals of the form to which conversion occurs. See Bernstein, *supra*, at 90–91. A single tiny crystal, constituting a single seed, might induce conversion. *Id.* at 91.

The first two factors that I have discussed under the rubric of "disappearing polymorphs" together provide the most persuasive explanation for the initial appearance of a new polymorph, while the first and third provide the most persuasive

explanation for the "disappearing polymorphs" phenomenon itself. The creation of the new polymorph is likely to make the laboratory or plant where it is produced seeded, with the result that efforts to produce the old polymorph may instead produce the new one, since it is the more stable form. In principle it should be possible to re-create the old polymorph, just by replicating the exact procedure by which it used to be created, only this time in a seed-free environment. Although it is difficult, and in some cases it may be impossible (paroxetine hydrochloride hemihydrate may be one of those cases—no one knows), to destroy all the seeds in seeded premises, crystalline seeds, unlike the pods in *Invasion of the Body Snatchers,* do not traverse galactic distances under their own power. Unless they are carried in samples or on a person's clothing from one seeded premises to another, the new premises will not be seeded and so it should be possible to re-create the old polymorph there. But this, as Dr. Bernstein explained, is in principle; and in practice efforts to re-create old polymorphs do not always succeed, probably because the critical mass of molecules that is required to cause conversion is so minute. In his book, Dr. Bernstein suggests that "a few tens of molecules" may be the minimum for conversion. Bernstein, *supra,* at 91. He was writing about polymorphs in general rather than about paroxetine, but it was implicit in Bernstein's testimony and also that of Dr. Byrn, and not persuasively countered by Apotex's expert witnesses, that the critical mass of paroxetine hydrochloride hemihydrate crystals required to induce conversion in a batch of anhydrous paroxetine is probably of the same order of magnitude (or minitude). Even if a seed required not ten but ten million molecules, a particle at the limit of visual detection would contain enough paroxetine hydrochloride hemihydrate to make more than one hundred million seeds. And there is no method of ventilation or fumigation that will eliminate all the hemihydrate crystals from a manufacturing environment.

Dr. Bernstein testified that if Apotex, desperate to avoid a charge of infringement, built a new plant in Antarctica where no hemihydrate seeds had ever been and started manufacturing anhydrate there, and a depressed worker in the plant

dropped a Paxil on the floor, the result might be to seed the plant and make it impossible from then on to produce pure anhydrate there. For that matter, he might have dropped it on the floor of his bathroom at home, releasing crystals that adhered to his skin or clothing. Bernstein described a remarkable episode involving the AIDS drug ritonavir, another polymorphic crystal. See also Sanjay R. Chemburkar *et al.*, "Dealing with the Impact of Ritonavir Polymorphs on the Late Stages of Bulk Drug Process Development," 4 *Organic Process Res. & Dev.* 413 (2000). Abbott began commercial production of the drug in 1996. Two years later a previously unknown—and, characteristically, a more stable—polymorph (Form II) appeared in the plant in the United States in which the final product was being manufactured. Immediately the old polymorph (Form I) began converting to the new. This precipitated a "market crisis," *id.* at 413, because unlike anhydrous and hemihydrous paroxetine crystals, Form I and Form II ritonavir were not bioequivalent. Fortunately (or so it seemed), Form II (the new polymorph) had not yet been observed in the plant in Italy where the bulk ritonavir was produced—but shortly after a visit to that plant by scientists who had been exposed to Form II, Form II showed up there too, probably (Bernstein omitted the qualification) as a result of seeding from Form II crystals on the scientists' clothing. Eventually Abbott was able to produce a version of Form I that would not convert—entirely; but the new version did contain up to 3 percent of Form II. *Id.* at 417.

Because the mechanism of seeding—the process, occurring at the atomic level, by which contact between the more and the less stable polymorph causes the latter to convert to the former—has not yet been discovered, Apotex argues that there is no scientific basis for believing that seeding occurs. But this is obviously wrong. Many scientific phenomena are identified before their causal mechanism is understood. Newton was distressed that he could not identify the causal mechanism behind the law of universal gravitation, which he had discovered, because according to that law bodies at a distance, with no intermediate links, were exerting force on each other.

Seeding appears to have been at work in Alan Curzons' laboratory. One might have supposed that the unexpected result of his experiment had been produced by the exact combination of steps that Curzons had taken in the making and crystallizing of paroxetine, including the choice of solvent to precipitate crystallization. But no; he soon discovered that it was very easy, using a variety of solvents, to produce hemihydrate—and the likeliest explanation is that the first batch of hemihydrate that he created had seeded his lab.

This leaves unexplained, however, why his initial experiment resulted in hemihydrate. Remember that he was not trying to produce a hemihydrate; the result of the experiment was serendipitous. One possibility is that as a result of the progress of technology, whereby over time the proportion of impurities in manufactured products diminishes, the chemical mixture on which he performed his experiment was so far free from impurities that the same application of solvent that had previously produced only anhydrous crystals now produced hemihydrate ones. Another possibility is that batches of paroxetine shipped from Harlow to Worthing had already seeded Curzons' lab because the manufacturing process at Harlow had, though without anyone's knowing it, already produced hemihydrate. For, once alerted by the outcome of Curzons' experiment to the existence of the hemihydrate, SmithKline discovered that a batch of paroxetine produced at Harlow in December 1984 (HP 23) and another batch produced there in the following month (HP 24) had both been hemihydrate. As SmithKline states in its post-trial brief, "no one knows for sure" how these early batches (including Curzons') "came to be crystalline paroxetine hydrochloride hemihydrate."

Nevertheless Dr. Bernstein testified that he was "absolutely convinced" that no hemihydrate had existed before December 1984. At first glance his testimony appears to lack any scientific basis. Because paroxetine does not exist in nature but, so far as anyone knows, was created for the first time in the early 1970s by Ferrosan, the hemihydrous form could not have existed before then. But it could have come into existence at any time between then and December 1984. It was not *detected* until March 1985, but existence and detection are

tected until March 1985, but existence and detection are not the same thing, for we know that HP 23 and HP 24, which are conceded to be hemihydrate, predated the earliest detection of hemihydrate, which was by Curzons in March 1985. The methods available as late as 1985 did not enable detection of small quantities of the hemihydrate in a mixture—smaller than 5 percent at the most. Smaller quantities may have existed ever since the first paroxetine was created.

Bernstein thought not, however, and gave two reasons. First, a batch of anhydrate manufactured by Ferrosan in 1980, though stored in a hot and humid place (the greater the heat—short of the melting point, of course—and the humidity, the likelier is conversion from the anhydrous to the hemihydrous form), had three years later still not converted to the hemihydrate form, suggesting that it had not been seeded and hence that there were no seeds as late as 1980. And HP 22, manufactured just weeks before HP 23, contained no detectable hemihydrate, whereas HP 23 was entirely hemihydrate. This is evidence that hemihydrate seeds can "metastasize" at a high rate when they come into contact with anhydrate crystals. If so, the fact that HP 23 was the first paroxetine in which the hemihydrate was detected is evidence that there were no seeds before then, that is, before December 1984, and almost certainly not when Ferrosan obtained its patent in 1977. It is true that Curzons in a 1985 memo reported having discovered hemihydrate in a Ferrosan batch dating from 1980, but quite apart from the possibility of later seeding, Curzons convincingly explained that he had been mistaken.

Dr. Terence Threlfall, Apotex's expert on polymorphism, testified to the contrary of Bernstein that anhydrous and hemihydrous forms of paroxetine can coexist happily. There is support for this conjecture in SmithKline's own evidence, of which more later, that some of Apotex's anhydrous product contains small amounts of hemihydrate without conversion of the rest. In other words, as Threlfall testified, a mixture of anhydrate and hemihydrate can be an equilibrium, in which event the earliest batches of paroxetine manufactured by Ferrosan may have contained undetectable quantities of the

hemihydrate. In light of this evidence, Dr. Bernstein's absolute certainty that hemihydrate did not exist before December 1984 is not tenable. No one knows when the hemihydrate form of paroxetine came into existence, although it is a reasonable inference that it did not exist in a detectable amount until then.

The conflicting testimony of Bernstein (and also Byrn) on the one hand and of Threlfall on the other can largely be reconciled on the following hypothesis: while the presence of hemihydrate seeds in a batch of anhydrate is likely, provided the ambient humidity and temperature are no lower than is normal in the temperate zone, to produce conversion within a short time, once the amount converted reaches a few percent of the mixture further conversion is unlikely without substantially greater humidity, temperature, or pressure. In other words, if conversion is plotted against time, then in the case of paroxetine hydrochloride as in the case of the revised process for producing Form I ritonavir, one will observe rapid growth from an initial very low level, followed by a leveling off at a few percentage points. This of course is under *controlled* environmental conditions; given enough humidity, heat, etc., conversion may continue until it reaches 100 percent. By the same token, with much tighter controls less, maybe no, conversion will take place despite the presence of seeds; the clearest case is where there are no water molecules in the environment of the anhydrate.

The Patent and the Patent Controversy

Crystalline paroxetine hydrochloride hemihydrate, along with certain processes for making it (none challenged by Apotex as invalid or contended by SmithKline to be infringed), was patented in patent 723 in 1988, the patent application having been filed in October 1986. After running the FDA gauntlet, the product was placed on the market under the name Paxil in 1993. The patent will expire, as I noted, at the end of 2006. In 1998 Apotex filed an ANDA in which it proposed to manufacture an anhydrous crystalline form of the paroxetine hydrochloride crystal, patent 196 having expired in 1992. Several other generic manufacturers have since filed ANDAs for vari-

ous anhydrous forms of paroxetine. Apotex was eager to be first because the generic manufacturer whose ANDA is the first to be approved obtains a 180-day period of exclusivity, see 21 U.S.C. § 355(j)(4)(B)(iv)—180 days during which he and the patentee (if as here the patent on the bioequivalent original has not expired) are in effect duopolists. SmithKline deplores Apotex's eagerness to be first but of course that eagerness is the mirror of SmithKline's zeal to obtain the much more extensive protection conferred by a patent that excludes the competition of a bioequivalent drug as infringing.

The reason Apotex waited as long as it did after the expiration of Ferrosan's patent to file its ANDA is that the FDA forbids submission of an ANDA on a "new chemical entity," which crystalline paroxetine hydrochloride hemihydrate is, or its bioequivalent (i.e., the anhydrate), until five years after the patented drug has been put on the market. 21 U.S.C. § 355(c)(3)(D)(ii). The hemihydrate wasn't *really* that new, being bioequivalent to its predecessor, the paroxetine patented by Ferrosan, but it was deemed new because the FDA had never approved the predecessor. See also 21 C.F.R. § 314.108.

As required, the ANDA specified the process of manufacture that Apotex would use to make the product in commercial quantities, and the site, actually sites, of manufacture. The bulk material (the crystalline paroxetine hydrochloride anhydrate before being mixed with excipients and made into pills) would be manufactured in a plant owned by an affiliate of Apotex named Brantford Chemicals, Inc. (BCI). It would then be shipped to a plant owned by another Apotex affiliate, TorPharm, where excipients would be added and mixed, the mixture compressed into pills, and the pills sprayed with an aqueous (88 percent water) coating and bottled for sale. The ANDA represented that Apotex's anhydrous version of crystalline paroxetine hydrochloride would not infringe patent 723. Disagreeing, SmithKline brought this suit, while meanwhile scurrying to obtain patents on other anhydrous polymorphs of the paroxetine hydrochloride crystal; these patents are involved in other litigation between it and Apotex. Since 1998, when Apotex filed its ANDA, SmithKline or its affiliates have applied for

almost 100 patents on paroxetine, though not all, or even most, are on anhydrous forms of the molecule.

It may seem odd that SmithKline could obtain *any* patents on anhydrous paroxetine hydrochloride given the expiration of the Ferrosan patent. However, that patent did not refer to paroxetine hydrochloride or to crystallinity, but to a set of compounds of which paroxetine maleate (another paroxetine salt) was one example; and the maleate probably was in amorphous (noncrystalline) form. So there may be room for patents on other salts or other crystals of anhydrous paroxetine. But that is not an issue in this case and I intimate no view on it. Whether manufacturers of brand-name drugs are using follow-on patents to compete unfairly with the generic manufacturers is at present under investigation by the Federal Trade Commission (described in an amicus brief that the FTC filed on January 28, 2003, in *SmithKline Beecham Corp. v. Apotex Corp.*, No. 99–CV–4304 (E.D. Pa.)), but played no role in the trial of this case.

In pretrial discovery SmithKline obtained samples of crystalline paroxetine hydrochloride anhydrate manufactured by Apotex and submitted them for testing to two academic scientists who testified for SmithKline, Dr. David Batchelder and Dr. Thomas Niemczyk. They testified that they had found hemihydrate in the samples and on the basis of this and other evidence SmithKline contends that the manufacture of the anhydrous product by Apotex is likely to infringe patent 723 because some of Apotex's output will consist of hemihydrate. According to SmithKline, the BCI plant is seeded with hemihydrate crystals because it was there that Apotex, exercising the broadened experimental-use privilege conferred by the Hatch-Waxman Act, used and made hemihydrate in the course of developing its anhydrous product. Any seed-bearing bulk material produced by BCI will, moreover, be formed into pills by TorPharm; and SmithKline argues that the compression exerted on the bulk material to make pills, together with the temperature and humidity in the plant and the fact that the final stage of manufacture involves the application of a water-

based coating, will promote further conversion of the anhydrous to the hemihydrous form of paroxetine hydrochloride.

Although crystals of paroxetine can be seen by means of an electron microscope if the crystals are "trapped" on the microscope's stage, there is no technique for detecting minute crystals in particulate matter in a pharmaceutical plant, on a worker's clothing, etc. But it does not follow, as Apotex unguardedly suggests, that the presence of such crystals, the "seed" crystals, cannot be inferred. What is true and important, however, is that the presence of slight amounts of hemihydrate in Apotex's product would not "do anything" for Apotex. The anhydrate has the identical therapeutic properties as the hemihydrate; that is entailed by their bioequivalence, which SmithKline does not contest. And although hemihydrate handles better in the manufacturing process because it is not hygroscopic, this will confer no cost savings on Apotex in the quantities in which it will be present (if at all) in Apotex's product. Dr. Joseph Robinson, an expert on pharmaceutical manufacturing, testified without contradiction that the percentage of hemihydrate in an anhydrate mixture would have to be in the "high double digits" to contribute any commercial value to the mixture. From Apotex's standpoint, any hemihydrate that happens to turn up in its product is a useless byproduct of a manufacturing process that, consistent with the "disappearing polymorphs" theory, is difficult or perhaps even impossible to conduct without producing tiny amounts of the unwanted byproduct. Dr. Bernstein testified that Apotex was indeed trying to manufacture an anhydrous product, while another of SmithKline's expert witnesses, Dr. Batchelder, testified that hemihydrate in an anhydrous product is an "impurity" and SmithKline's lead counsel described anhydrate that contains some hemihydrate as "degraded."

Validity and Claim Construction

There is no infringing an invalid patent. A number of Apotex's challenges to the validity of patent 723 were rejected by Chief Judge Kocoras in pretrial rulings that I am not disposed to reexamine. What is left is, first, a frivolous argument that

either patent 196, or an early article that discussed the paroxetine molecule, R. Battegay, M. Hager & U. Rauchfleisch, "Double-Blind Comparative Study of Paroxetine and Amitryptyline in Depressed Patients of a University Psychiatric Outpatient Clinic (Pilot Study)," 13 *Neuropsychobio.* 31 (1985), or both, "literally" (as distinct from "inherently," discussed next) covered the hemihydrate form. There is no mention of hemihydrate in the patent or in the article and the hemihydrate polymorph of paroxetine was unknown either when the patent application was filed or in 1977 when the patent was granted. Nor has Apotex shown that hemihydrate, the invention claimed by patent 723, was obvious given the prior art (patent 196 and the Battegay *et al.* article).

A more plausible argument is that the hemihydrate form was inherent in patent 196 because anyone who followed the directions in that patent would inevitably produce hemihydrate. If it was inherent, it is deemed anticipated, and patent 723 would be invalid. *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999); *In re Robertson, supra*, 169 F.3d at 745. Although it was not until seven years after patent 196 was granted that SmithKline chemists at Harlow, and Alan Curzons at Worthing, while following more or less the directions in the patent, produced hemihydrate, the hemihydrous form of paroxetine may have existed earlier and if so the fact that it was not recognized earlier would not defeat a defense of inherency. *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999); *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1348 (Fed. Cir. 1999); *Abbott Laboratories v. Geneva Pharmaceuticals, Inc.*, 51 U.S.P.Q.2d 1301, 1305–06 (N.D. Ill. 1998), aff'd, 182 F.3d 1315 (Fed. Cir. 1999). But Apotex has failed to prove this by clear and convincing evidence, as required to invalidate a patent. The serendipitous appearance of a polymorph years after another polymorph of the same crystal is patented does not prove to the requisite degree of certainty that the new polymorph was inherent in the old. In this respect the uncertainties in the scientific community concerning the provenance and causality of polymorphs aid SmithKline because of the heavy burden of proving invalidity coupled with

the narrowness with which the Federal Circuit defines inherency. Inherent anticipation "may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *MEHL/Biophile Int'l Corp. v. Milgraum, supra,* 192 F.3d at 1365 (emphasis in original); see also *In re Robertson,* 169 F.3d 743, 745 (Fed. Cir. 1999); *Glaxo Inc. v. Novopharm Ltd.,* 52 F.3d 1043, 1047–48 (Fed. Cir. 1995); *Continental Can Co. USA, Inc. v. Monsanto Co.,* 948 F.2d 1264, 1268–69 (Fed. Cir. 1991).

I have been assuming so far that inherent anticipation requires that practicing the old patent invariably produce the new product (the product that is the subject of the challenged patent—here, the hemihydrate—and is contended to have been inherent in the practice of the old patent) *from the moment the old patent was issued.* This may be too strenuous a requirement, though I cannot find any case one way or the other on the point. Maybe it is enough if, because of widespread seeding, by the critical date for anticipation (October 1985, one year before SmithKline applied for patent 723, see 35 U.S.C. § 102(b)) no one who followed the steps outlined in patent 196 for making paroxetine would fail to produce at least some hemihydrate. And this is possible. But again the burden of proof on the issue of validity saves SmithKline. For it is equally possible, as far as anyone knows, that practicing patent 196 in non-seeded premises—and goodness knows there were some in the United States as of that date—would not have produced any hemihydrate. Cf. *Glaxo, Inc. v. Novopharm Ltd.,* 830 F. Supp. 871, 875–77 (E.D.N.C. 1993).

Apotex has still another arrow in its invalidity quiver, however, and that is the argument that the description of claim 1 of patent 723, the only claim in issue, is too indefinite. A patent's specification (the descriptive part of the patent) must "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112; see, e.g., *Beachcombers v. Wildwood Creative Products, Inc.,* 31 F.3d 1154, 1158 (Fed. Cir. 1994). Claim 1 states simply: "crystalline paroxetine hydrochloride hemihydrate." SmithKline argues that

this means what it says, so that even if Apotex's generic paroxetine product contains only a single crystal of the hemihydrate, an undetectable quantity, claim 1 will be infringed. SmithKline correctly notes that the reference group for claim construction is limited to persons knowledgeable about the relevant technology—chemists in this case—and that the four words constituting claim 1 are each of them perfectly clear to chemists and that the four words taken together are also clear to them, at least as a matter of literal interpretation.

Yet until completion of the portion of the trial devoted to the issue of validity SmithKline equivocated between the literal interpretation and a looser interpretation that would add the words "in a detectable amount" to the end of claim 1, or (a reading it preferred) "in a detectable amount whether or not detectable by the methods available when the invention was made or the patent applied for or granted." Eventually, however, though reluctantly, it committed itself to the "single crystal" interpretation, according to which "crystalline paroxetine hydrochloride hemihydrate" includes *all* manifestations of the hemihydrate, no matter how or where produced, or in what quantity relative to the mixture of which it is a part; even if the production was inadvertent, unavoidable though undesired, and wholly without benefit to the producer or detriment to SmithKline in the sense of cutting into SmithKline's market; and even if the amount is so tiny as to be beyond the limits of detection of any instrument present or foreseeable and the product in which it unexpectedly pops up does not compete with anything made or sold by SmithKline. It need not even be a drug. According to SmithKline, if a worker in a chocolate factory popped a Paxil into his mouth and as a result the factory became seeded with hemihydrate crystals, and the seeds found their way into chocolate that was then sold, the sale would infringe patent 723. (Actually this is wrong; the "first sale" doctrine would allow the worker to do anything he wanted with Paxil tablets that he had bought. The example is saved by assuming that the source of the seeds is a SmithKline executive who picked them up while visiting a seeded SmithKline facility and later visited the chocolate factory.) If the BCI factory is

seeded, as it appears to be, all the other drugs that BCI manufactures there, some two dozen or so, may be seeded too and all are thus infringing (if SmithKline's interpretation of claim 1 is correct and does not invalidate the claim) and the company has a slew of additional patent-infringement suits to bring.

This is heady stuff; someone not steeped in patent law might think it loony; and it is not surprising that SmithKline equivocated before embracing the single-crystal theory (embracing it perhaps out of fear that otherwise its proof of infringement would fail—as indeed it would, as we'll see). It continued until the end of the trial to duck and feint by arguing that whether patent 723 claims single crystals is "academic," either because infringement cannot be proved if the infringing component of a mixture is below the limits of detection or because injunctive relief, as in my chocolate example, would be inequitable. The second point is a potentially fatal concession, as I shall point out later. The first is wrong. Being able to detect the presence of hemihydrate seeds by instruments and being able to infer their presence from circumstantial evidence are not the same. To equate them is a variant of Apotex's erroneous belief that if seeds cannot be "seen" there is no scientific basis for supposing them, or the phenomenon of seeding, to exist.

SmithKline insists that my chocolate hypothetical is "not this case." It is not. But one tests a definition by considering all the things it covers, its "extension" as philosophers say. If someone challenges a definition of "swan" as any bird with a long neck by pointing out that flamingos have long necks, it is no answer that the person offering the definition is not interested in flamingos. It is still an overinclusive definition. SmithKline may not interpret its claim narrowly to avoid invalidity and broadly to prove infringement. *Unique Concepts, Inc. v. Brown*, 939 F.2d 1558, 1562 (Fed. Cir. 1991).

Reference to hypotheticals does not violate the principle that "claims may not be construed by reference to the accused device." *NeoMagic Corp. v. Trident Microsystems, Inc.*, 287 F.3d 1062, 1074 (Fed. Cir. 2002). As the Federal Circuit had explained in an earlier case, "A claim is construed in the light of

the claim language, the other claims, the prior art, the prosecution history, and the specification, not in light of the accused device. ...[C]laims are not construed 'to cover' or 'not to cover' the accused device. That procedure would make infringement a matter of judicial whim. It is only after the claims have been construed without reference to the accused device that the claims, as so construed, are applied to the accused device to determine infringement." *SRI Int'l v. Matsushita Electric Corp. of America*, 775 F.2d 1107, 1118 (Fed. Cir. 1985) (en banc). In other words, the judge is not to say, "I can make everybody more or less happy by first examining the accused infringer's invention and then narrowing the patentee's claim so that it just excludes the defendant's invention, leaving the patent claim otherwise intact." But disallowing that method of claim construction does not exclude consideration of hypothetical cases as an aid to determining the scope of the claim. My objective is not to protect chocolate makers from being dragged into court by SmithKline (a most improbable prospect, and one which SmithKline expressly disclaimed in its post-trial brief), but to decide whether the claim has limits that render it definite.

The "single crystal" interpretation of claim 1 may be extravagant, but it is not *completely* ridiculous, whatever a layperson might think. The claim is of a product rather than of a method of production; and to make the patentability of a product depend on the percentage of the patented product in a mixture would lead to absurd results. The paroxetine in Paxil is mixed with excipients that constitute 90 percent of the pill by weight, yet no one supposes that the relative weight of the paroxetine in the pill has the slightest significance for patentability. Unlike copyright law, moreover, patent law does not recognize a defense of independent creation. The fact that if Apotex does create hemihydrate as a byproduct of its attempt to manufacture public-domain anhydrate it will not be deliberately "copying" SmithKline is irrelevant.

But there are mixtures and there are mixtures. In a previous order in this case, which SmithKline applauds for holding that hemihydrate does not forfeit patent protection merely by

being mixed with something else, Judge Kocoras stated: "It does not necessarily follow, however, as SmithKline would have us believe, that claim 1 covers any modicum of hemihydrate found in any mixture with other substances or polymorphic forms." *SmithKline Beecham Corp. v. Apotex Corp.*, No. 98 C 3952, 2001 U.S. Dist. LEXIS 19766, at *43 (N.D. Ill. Nov. 30, 2001). He went on to say that he thought the claim could be construed in a way that would preserve its validity when read in light of the patent specification, citing *Exxon Research & Engineering Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001). He pointed out that some of the properties specified, such as higher melting point, greater stability, and nonhygroscopicity, "distinguish the new material from prior art anhydrate and thus establish its patentability." *SmithKline Beecham Corp. v. Apotex Corp.*, *supra*, at *45. And he said that he thought there was enough information in the specification to be able to construct a definite meaning for claim 1 and thus save the patent's validity. It falls to me to find that meaning. *Id.* at *47.

Were claim 1 to be interpreted as broadly as SmithKline now contends, it would fail for indefiniteness. (I emphasize that this is not an issue that Judge Kocoras even reached, let alone decided in SmithKline's favor.) The purpose of the statutory requirement of definiteness is to place the members of the relevant technical community on notice of the scope of the patent so that they don't infringe it inadvertently. *General Electric Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 369 (1938); *McClain v. Ortmayer*, 141 U.S. 419, 424 (1891); *All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 309 F.3d 774, 779–80 (Fed. Cir. 2002); *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1378–79 (Fed. Cir. 2000). For remember that inadvertency is not a defense to infringement; there is no defense of independent creation. "The primary purpose of this requirement of definiteness in claims is to provide clear warning to others as to what constitutes infringement of the patent," 3 Donald S. Chisum, *Chisum on Patents* § 8.03, p. 8–18 (2002), because "a zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage

invention only a little less than unequivocal foreclosure of the field." *United Carbon Co. v. Binney & Smith Co.*, 317 U.S. 228, 236 (1942), quoted in *Exxon Research & Engineering Co. v. United States*, *supra*, 265 F.3d at 1375. Stated differently, "if patent infringement can be compared to trespassing, the claims serve as the boundary markers that define what is, or is not, an encroachment on the inventor's exclusive territory." Alan L. Durham, *Patent Law Essentials: A Concise Guide* 66 (1999).

This purpose cannot always be fulfilled by a literal interpretation. The ordinary meaning of a word can deprive a claim of clarity. *Northern Telecom Ltd. v. Samsung Electronics Co.*, 215 F.3d 1281, 1291 (Fed. Cir. 2000). And context can ambiguate as well as disambiguate. Claim 1 must be read against the background of the specification. *Solomon v. Kimberly-Clark Corp.*, *supra*, 216 F.3d at 1378; *In re Moore*, 439 F.2d 1232, 1235 and n. 2 (CCPA 1971). SmithKline acknowledges in its post-trial brief that patent claims are to be interpreted in light of "the patent's specification" as well as the claims language. Patent 723's specification points out the superior handling characteristics of the hemihydrate in the manufacture of a paroxetine salt for therapeutic purposes. This would lead a reader, however technically adept he might be, to suppose that the patented invention was of a crystalline form constituting the active ingredient of a paroxetine-based drug. He would not think the claim extended to the involuntary creation of the crystalline form in quantities so minute as to be of no therapeutic, manufacturing, or other commercial significance and indeed to be undetectable by any means known at the time the patent was applied for and was issued. There is no hint of such a possibility in the patent; the landmine that SmithKline now wants to explode under Apotex is concealed. (Not concealed from Apotex, though, whose CEO expected from the start that SmithKline would sue it.)

An adequate description of claim 1, if indeed the claim embraces even a single crystal created by adventitious seeding, would warn the world of such dangers as are conjured up by the chocolate example. The example may seem fantastic but

the reality is alarming enough—as the ritonavir episode recounted by Dr. Bernstein (SmithKline's own witness, remember) illustrates—for any firm contemplating manufacture of a crystalline paroxetine hydrochloride anhydrate, even though it is a public-domain product. "If claim language is vague, competitors must proceed at their peril, and the uncertainty provides the patent owner with what is, in effect, a broader claim." Durham, *supra*, at 68. Not knowing how far claim 1 reaches, competitors might steer clear of producing a product that would infringe the patent under the patent's broadest possible interpretation. And not just competitors, as we know from the chocolate example. There would be the kind of "chilling" effect of which the courts speak when they are considering First Amendment challenges to vague or overbroad regulations of speech.

Suppose that Apotex, reasonably assuming that no one could claim with a straight face that a single crystal inadvertently created as a result of accidental seeding would make Apotex an infringer of claim 1 of patent 723 and thus prevent the FDA from granting its ANDA, spent a billion dollars on making sure that BCI would produce no more than 100 molecules of hemihydrate in any batch of its anhydrate product. Would it be unreasonable in interpreting claim 1 as not claiming for SmithKline the exclusive right to those molecules? I think not. I am not even sure that SmithKline would disagree. Instead it probably would say that that is not our case either, because Apotex did not make *heroic* efforts to avoid producing even undetectable amounts of hemihydrate, as in my example. This point may bear on infringement but it does not bear on claim construction; to repeat, a patent claim is not definite if it does not make the claim's limits clear. I take SmithKline's equivocations to be tacit acknowledgements that those limits are not clear.

I am inclined, however, rather than to declare claim 1 invalid for indefiniteness to interpret it as excluding hemihydrate produced by involuntary conversion of a proportion of an anhydrous mixture so small as to lack any commercial significance. The Federal Circuit favors giving a claim a narrowing con-

struction to avoid invalidating it for indefiniteness, *Exxon Research & Engineering Co. v. United States*, *supra*, 265 F.3d at 1375–77; *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577 (Fed. Cir. 1984), even if the patent claim "poses a difficult issue of claim construction." *Exxon Research & Engineering Co. v. United States*, *supra*, 265 F.3d at 1375. My construction produces a claim with definite, readily observable boundaries because Apotex's manufacturing methods, and those of other producers of anhydrous forms of paroxetine, will produce hemihydrate, if any, in quantities far below the "high double digits" level at which hemihydrate in a mixture with anhydrate attains commercial significance. There is no risk of inadvertent infringement and hence of giving the patent an *in terrorem* effect beyond its valid scope, if my construction is correct.

In adopting the "any commercial significance" construction I am not converting a product claim to a process claim, because the patented invention remains the product whatever the process used to make it. Nor am I suggesting that the presence of trace elements of a patented product can never be infringement, for reasons illustrated by the facts of *Northern Telecom Ltd. v. Samsung Electronics Co.*, *supra*, on which SmithKline relies without acknowledging the wholly different situation described in that case. Nor am I taking undue liberties with the claim's "plain meaning." Literal interpretations that produce absurd results are regularly rejected in contractual and statutory interpretation, *Public Citizen v. Dept. of Justice*, 491 U.S. 440, 453–55 (1989); *Level 3 Communications, Inc. v. Federal Ins. Co.*, 168 F.3d 956, 958 (7th Cir. 1999); *Marlowe v. Bottarelli*, 938 F.2d 807, 812 (7th Cir. 1991); *Outlet Embroidery Co. v. Derwent Mills*, 172 N.E. 462, 463 (1930) (Cardozo, J.), and the Federal Circuit deems statutory interpretation a useful analogy to claim construction. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 987 (Fed. Cir. 1995), aff'd, 517 U.S. 370 (1996). The single-crystal interpretation of claim 1 has absurd consequences that do not serve any policy of patent law. "General descriptive terms will *ordinarily* be given their full meaning." *Johnson Worldwide Associates, Inc. v. Zebco Corp.*,

175 F.3d 985, 989 (Fed. Cir. 1999) (emphasis added). This is the rare case in which the qualification that I have italicized comes into its own, and for the reason stated in the case just cited: where the ordinary meaning of a term deprives a claim of clarity, rendering it indefinite. *Id.* at 990.

My approach to the interpretation of claim 1 is supported by the oldish but still goodish case of *Corning Glass Works v. Anchor Hocking Glass Corp.*, 374 F.2d 473, 475–79 (3d Cir. 1967). The patent covered crystallized glass (Corning Ware, which looks like porcelain) and described the product as being "at least" 50 percent crystalline. Apparently there was no way to measure the percentage of crystallinity precisely, and on that basis the district court held the patent unenforceable because he thought it would be too difficult for a competitor to determine whether its product was "at least" 50 percent crystalline) The court of appeals reversed. The court looked to the purpose of the invention, which was to create a "material with substantially different properties [from conventional glass], predominantly crystalline." There had been testimony that the percentage was not really the point; the point was the changed properties of the material compared to noncrystalline glass. And these were apparent on inspection. The court forwent literalism to uphold rather than defeat the patent's validity, and that is what I am doing here.

Even closer to the present case, in light of SmithKline's insistence that claim construction must never add words to the words of the claim, is *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477–78 (Fed. Cir. 1998). There, on the basis of the patent specification, the Federal Circuit held that "degradable" meant "degradable only by dissolution," though the additional words did not appear in the claim itself, but were added by construction. See also *Laitram Corp. v. Morehouse Industries, Inc.*, 143 F.3d 1456, 1463 (Fed. Cir. 1998); *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1350 (Fed. Cir. 1998).

Infringement

If the interpretation of claim 1 of patent 723 that I have adopted (crystalline paroxetine hydrochloride hemihydrate in any quantity sufficient to have any commercial significance) is sound, and claim 1 therefore valid, then it is clear that there is no infringement and the case is over. This makes SmithKline's victory on validity somewhat Pyrrhic, but only somewhat, since if the patent were invalid the generic manufacturers could make the hemihydrate form, whereas if they are confined to anhydrous paroxetine they have to reckon with SmithKline's imposing array of recently acquired anhydrate patents.

Noninfringement is easily shown under the narrow interpretation of claim 1 because SmithKline has failed to prove that even when Apotex increases production of its generic anhydrate to full commercial scale, if it is ever permitted to do so, the proportion of hemihydrate in the product is likely to exceed one or two percentage points, a level far too low to produce any benefits whatsoever to Apotex. (It hasn't even proved that the proportion of hemihydrate in Apotex's product will reach those levels, but that is for later.) But since the Federal Circuit may disagree with my interpretation and may also disagree that a broader interpretation would render claim 1 invalid for want of a definite description, prudence, coupled with the fact that the issue of infringement was fully tried, impels me to push on and, assuming that the patent is valid even when read broadly, decide whether patent 723 is likely to be infringed by the methods that Apotex intends to use to manufacture its anhydrous product. The burden of proof to show infringement is of course on SmithKline.

Whether SmithKline has proved infringement under the broadest, the "single crystal," interpretation of claim 1 could in principle (though not in practice) depend on the answer to the following esoteric legal question: if a single hemihydrate seed escaped from a Paxil tablet that was on BCI's premises in the mid-1990s, and it has been floating about BCI's plant ever since and it will find its way into a batch of anhydrous material that the plant produces and eventually into a pill that is sold to the public, would Apotex, though not guilty of infringing SmithKline's exclusive right to *make* the patented product, be

guilty of infringing either of the other rights that a patent confers, namely the right to use or the right to sell (or offer to sell) the patented product? 35 U.S.C. § 271(a). Maybe not. Quite apart from the first-sale doctrine that I mentioned in discussing the first version of the chocolate-factory hypothetical, Apotex would not be *using* the seed in any intelligible sense of the word, since hemihydrate in small amounts does nothing for the anhydrate with which it is mixed. And it would not be *selling* it in a meaningful sense either, since the presence of a single seed would not increase the value to consumers and hence the price that Apotex could charge for the anhydrate, or reduce Apotex's costs of production or sale, by even a Canadian penny.

I need not try to wrestle this question to the ground (though I note that if the answer is "no," it at least nixes the argument that the chocolate manufacturer in the second version of the hypothetical, the one to which the first-sale doctrine did not apply, would be infringing, for seeds of paroxetine hydrochloride hemihydrate will not convert chocolate to paroxetine hydrochloride hemihydrate). Its factual premise is unrealistic. If BCI produces bulk material that contains hemihydrate seeds, even in a very small number, some undoubtedly will be crystals that BCI made, rather than all being leftovers from mid-1990s experimental uses. It is true that BCI is trying to minimize the amount of hemihydrate that its production process creates—SmithKline's argument that Apotex is indifferent to the amount of hemihydrate its production process creates is unsound, because the more hemihydrate there is the more vulnerable Apotex is to charges of patent infringement. But because BCI's plant is seeded as a result of the mid-1990s experiments, and because the anhydrate as it proceeds through the process will at several junctures be exposed to air that contains enough water molecules to permit conversion of anhydrate to hemihydrate, BCI probably will be "making" at least some hemihydrate crystals and therefore infringing, at least prima facie, patent 723 if claim 1 is interpreted to cover single crystals of the hemihydrate. And although a handful of crystals in a batch of the anhydrate is not detectable in the sense that its presence can be determined by a test, I pointed out earlier

that the presence of a substance may be inferable even when it cannot be detected by instruments however sensitive. That is the situation here. *Some* conversion from anhydrate to hemihydrate is likely to occur in a seeded facility in which the anhydrate is exposed to air; BCI's plant is seeded; and the anhydrate manufactured there is exposed to nondehumidified air before it leaves the plant. This evidence is sufficient to support an inference that BCI will be making at least tiny amounts of the hemihydrate if it is permitted to manufacture the anhydrate. But I have rejected the "single crystal" interpretation of claim 1 of patent 723.

An intermediate interpretation between "single crystal" and "any commercial significance" deserves consideration, however. It is one that SmithKline has flirted with and will doubtless embrace as a fallback if my rejection of the single-crystal claim construction stands. The fallback interprets "crystalline paroxetine hydrochloride hemihydrate" as being limited to detectable amounts of the compound.

Such an interpretation makes the issue of infringement more complicated and uncertain than either of the other two interpretations that I have been examining. I must consider to begin with whether "detectable" means detectable when the patent was applied for back in 1986 (or in 1988, when the patent was granted, but nothing turns on the choice between these dates, though the only case I can find supports the earlier one, *Raybestos-Manhattan, Inc. v. Texon, Inc.*, 268 F.2d 839, 842 (1st Cir. 1959)), rather than today, when as a result of better methods the limits of detection are lower. It is true as Judge Kocoras ruled that to prove infringement a patentee is not limited to the means of detection that existed when the patent was issued, any more than the prosecution in a criminal case is forbidden to use a means of detection (say, a DNA test) that did not exist when the statute creating the offense was enacted or when the crime was prosecuted. But the question is not whether SmithKline can use new methods of detecting the presence of polymorphs to prove that Apotex's anhydrate will contain hemihydrate. It is whether "detectable quantities" should be limited to quantities of hemihydrate that were de-

tectable by the technology of the time. Someone who wanted to manufacture a product that did not infringe claim 1 could not make an informed decision on whether or how to proceed with his project were he at risk that unforeseen technological advances would result in his being declared an infringer. His uncertainty would deter innovation and thus offend patent policy. The "detectable back then" approach has the advantage that "it does not cause the patent to mean one thing at the time of its issuance and another at some later date upon the discovery of a more accurate test." *Id.* at 842.

Apotex is not an infringer under this interpretation of claim 1. When SmithKline obtained patent 723 the limit of detection of the hemihydrate when mixed with an anhydrate was between 5 and 8 percent. Apotex is unlikely to produce an anhydrate that contains such a high percentage of hemihydrate. True, if there are enough seeds, a sufficiently humid atmosphere, sufficient heat, strong pressure, and plenty of time, conversion to a higher percentage is likely. In an early experiment conducted by SmithKline, samples of anhydrate taken from HP 12—a batch that had been made before 1982, which in all likelihood was before the hemihydrate came into existence—were seeded with 2 percent and 4 percent hemihydrate. After the seeded samples were exposed for a week to a temperature of 37° Centigrade (99° Fahrenheit) and a relative humidity of 75 percent, conversion was observed—complete conversion with the 4 percent seeding and conversion to "largely" hemihydrate with the 2 percent seeding. P. C. Buxton, I. R. Lynch & J. M. Roe, "Solid-State Forms of Paroxetine Hydrochloride," 42 *Int'l J. Pharmaceutics* 135 (1988).

BCI studies of several batches made by it in 1997 showed small amounts of conversion to hemihydrate after nine months. These batches had been produced in a pilot operation, however, and Apotex presented persuasive evidence at trial that BCI's current manufacturing methods are less likely to cause conversion. SmithKline contends that experiments that Dr. Keshava Murthy, a chemist who is currently BCI's president, conducted on batches made in 2000 revealed conversion, but I reject the contention below. SmithKline also points to a sample from one

batch made by BCI in 2001 that it claims contains 75 percent hemihydrate. This is a real outlier, however—and an unconvincing one. The estimate comes from Dr. Niemczyk's eyeballing of the spectrum of the sample. When he was asked how one can determine the percentage of a particular substance in a mixture by merely a visual inspection of the mixture's spectrum, his answer was perfunctory and unconvincing. I conclude that no recent batches produced by Apotex have been reliably shown to contain hemihydrate at the limit of detection (5 percent) of the standard tests.

Remember that I have to make a *predictive* judgment: the issue is not, has BCI produced any hemihydrate, which unquestionably it has, if only when it was exercising its Hatch-Waxman rights, but will it do so (and here I am considering whether it will do so in a quantity equal to at least 5 percent of the anhydrate mixture) if and when it is permitted to go into full production. Apotex presented evidence that its current system of production, which incorporates a variety of measures designed to minimize conversion, such as minimizing the exposure of the anhydrate to air or other sources of water, will enable it to hold the percentage of the hemihydrate in its anhydrate product far below 5 percent. The ambient temperature will be much lower than 99° F, the relative humidity much lower than 75 percent, most of the production process will be conducted in vacuum-sealed reactors so that the aggregate period of exposure to the air will fall far short of 168 hours, and the quantity of seeds deposited in the paroxetine during the production process will be much less than 2 or 4 percent. Those figures are closer to the maximum plausible estimate of the level of hemihydrate *after* conversion by adventitious seeding notwithstanding a controlled environment.

SmithKline argues that scaling up from pilot production to full commercial production is bound to increase the likelihood and extent of conversion. Dr. Bernstein acknowledges, however, that little is known about the effects of scale-up on conversion. Bernstein, *supra*, at 256. And because Apotex has a powerful incentive to minimize the amount of hemihydrate in its commercial production in order to avoid future suits for in-

fringement, there may well be *less* hemihydrate in the scaled-up than in the pilot phase of production. And here uncertainty operates against SmithKline because the burden of proof on infringement rests on it rather than on Apotex. The burden is not carried by the recitation of generalities about humidity, pressure, heat, and seeds being the risk factors for conversion; they are the risk factors, but what is missing is a formula that would relate them, at the level they are likely to attain in BCI's mature production process, to the probability and amount of conversion.

SmithKline further argues, however, that even if the bulk anhydrate that BCI produces and ships to TorPharm for tableting will contain only seeds of the hemihydrate, the heat and humidity in the TorPharm plant, and particularly the pressure exerted on the bulk material to form it into tablets, will, if there are seeds in the bulk material, surely cause conversion to the hemihydrate in a higher percentage than 5 or 8. Beware "surely"; the evidence, presented by SmithKline's experts Byrn and Dr. Christopher Rhodes, is unconvincing. As in the case of BCI's production of the bulk material, with the burden of proving infringement on SmithKline the scientific uncertainties concerning polymorphism in general and the paroxetine polymorph in particular work against SmithKline rather than against Apotex. All Rhodes could say was that there would be heat, pressure, etc. in TorPharm's production process; he could not say how much. All Byrn could say was that the hotter the plant, the greater the pressure, etc., the more likely was conversion, but he could not say how much more likely or what percentage of the paroxetine in the final tablets would be hemihydrate. We know that moisture is a necessary condition for conversion of the anhydrate and also that at pressures much higher than anything likely to be encountered in Apotex's tableting process the combination of seeds, adequate moisture, and pressure constitutes a set of sufficient conditions for conversion to occur. Even in that case, however, we do not know how much conversion will occur. And no evidence was presented that would permit an inference, when the pressure does not reach the critical level, that Apotex is more likely than

not to produce an anhydrate mixture that contains more than 5 percent hemihydrate.

SmithKline did not seek to conduct tests in BCI's or TorPharm's plant to determine whether the manufacture of the bulk or finished anhydrate would create hemihydrate. It could have gotten a court order allowing it to do so, had Apotex balked. And in jousting with BCI's Dr. Murthy over the latter's testimony that a finding of hemihydrate in a test of the anhydrate was a false positive, SmithKline's lawyer acknowledged that adventitious seeding is a hit-and-miss phenomenon. The test in question had been repeated because the positive result was unexpected (not to mention undesired!). The retest revealed no hemihydrate and this led Murthy to conclude that the first result had yielded a false positive. The lawyer countered by remarking that the first test might still be evidence of seeding, because seeding might have affected only the first test: "Sir, isn't it quite possible that the seed was in the laboratory on that day when you measured it, but the seed wasn't on the testing pan the next time you measured it?" This insinuation undermines SmithKline's theory that once there are seeds in a facility, conversion to detectable levels of hemihydrate is highly likely even if precautions are taken, such as minimizing exposure to air, controlling temperature, humidity, and the force of compression, and adding desiccants.

Murthy also testified about the results of repeated tests on another batch. The first test had been conducted three months after the batch was created and was positive for hemihydrate. The test was immediately redone and was negative. The test was repeated at six months with a negative result, 12 months (positive), and 18 and 24 months (both negative). Murthy thought the two positive test results must have been false positives because if a batch reveals conversion at time t more conversion can be expected at any subsequent time; almost all the tests in evidence in this case showed more conversion the greater the lapse of time since the anhydrate being tested was produced and none showed conversion declining with time. The lawyer challenged Murthy by suggesting that the tests might have been on samples from different locations in the barrel of

anhydrate. Maybe so, but this implies that the hemihydrate and the anhydrate can coexist in an equilibrium.

I also find it significant in predicting how much hemihydrate is likely to be found in Apotex's product that SmithKline did not commission or conduct any controlled experiments on seeding. It could have found a facility in which hemihydrate seeds were unlikely to be present, made anhydrate there, let the anhydrate sit around long enough to indicate that it wasn't going to convert (this would be evidence that the facility was indeed unseeded), then made the hemihydrate and then the anhydrate again and see whether and when and under what environmental conditions of heat, pressure, humidity, and impurities and to what extent (5 percent? 50 percent? 100 percent?) it converted to hemihydrate. SmithKline also failed to test all the samples of Apotex's product, both bulk material and pills, that Apotex produced in response to SmithKline's discovery requests, and I never got a satisfactory answer as to how the selection was made. SmithKline also failed to conduct more than one type of test on any sample (with an irrelevant exception involving some DSC tests that Dr. Byrn conducted with inconclusive results), although multiple testing is *de rigueur* when seeking to identify a substance that is only a small part of a mixture that contains closely related substances (such as different polymorphs of the same, or nearly the same, molecule). And it did not follow through on Dr. Bernstein's suggestion as to how one might try to re-create a less stable polymorphic form after a new, more stable form had appeared. Bernstein, *supra*, at 93. Of course Apotex could have done more testing too, but in a finger-pointing contest SmithKline must lose because it bears the burden of proving infringement.

At trial SmithKline repeatedly found itself coming and going on the question whether Apotex's product is likely to contain at least 5 percent hemihydrate. To refute Apotex's claim that if its product contains *that* much hemihydrate Ferrosan's must have contained *some* and so hemihydrate was invented and indeed patented in patent 196 and therefore could not be patented later, SmithKline effectively refuted the inconclusive spectroscopic evidence (which focused on the "Jacewicz shoul-

der" and the "Niemczyk tail," ambiguous indications of the presence of hemihydrate in infrared spectra) that Apotex presented with regard to hemihydrate in Ferrosan's anhydrous product. The same inconclusiveness, however, dogged SmithKline's effort to establish by conventional methods (that is, the methods that have a 5 to 8 percent limit of detection, such as visual inspection of infrared spectra, x-ray powder diffraction studies, and differential scanning calorimetry) that either bulk material or pills produced by Apotex contain that much hemihydrate.

In sum, I am not persuaded that Apotex will produce an anhydrate that has sufficient hemihydrate to be detectable by the methods in use in 1985. But now suppose that "detectable amounts" in the "detectable amounts" interpretation of claim 1 means detectable by any method, however recent. (So here is a fourth possible construction of claim 1 that I am considering.) This interpretation would raise a serious question of indefiniteness, though one I shall not try to answer. As science develops finer and finer instruments for the detection of polymorphs, the "detectable by any means" and "single crystal" interpretations approach convergence. A claim construction that places a potential infringer at the mercy of scientific advances that may be unpredictable suffers from the same infirmities as the single-crystal interpretation and therefore might if adopted invalidate the patent. But I shall limit my consideration to the question whether SmithKline has proved infringement under this interpretation of claim 1.

Two of SmithKline's expert witnesses, Drs. Niemczyk and Batchelder, claimed to have detected hemihydrate in samples of Apotex's anhydrate product in amounts below the old 5–8 percent limit of detection. Niemczyk used a statistical technique called "partial least squares" that is designed to extract more information from a spectrum than any of the older methods. Apotex tried to convince me that it is an unproven method and was misapplied by Niemczyk. I reject the first point. Partial least squares has in recent years become a standard method for detecting the presence of a specific crystalline form. See *Glaxo, Inc. v. TorPharm, Inc.*, 153 F.3d 1366, 1373 (Fed.

Cir. 1998). Dr. Niemczyk is an experienced practitioner of it but I do not credit his testimony that he was able to detect small amounts (down to a tenth of one percent) of hemihydrate in five of the nine samples of Apotex's anhydrate that he tested.

The first step in using PLS to determine the composition of an unknown mixture is to create a reference sample (or samples) comprising a mixture of known proportions of known substances. The spectrum of that mixture (an infrared spectrum in this case, though PLS can be applied to other spectrographic methods as well) is then compared with the spectrum of the mixture whose composition is sought to be determined. A visual comparison of spectra will not detect an amount of hemihydrate smaller than 5 percent of a mixture with anhydrate. This is where PLS comes in.

The key concepts in PLS analysis are "factors," "degrees of freedom" (each degree of freedom corresponds to one causal or explanatory variable), and "spectral F ratios" (a measure of statistical significance). Each substance in a mixture will generate its own spectrum, making the spectrum of the mixture a composite. With the aid of a computer, the PLS analyst "factors" the composite spectrum into its components, much as one would factor a number. Niemczyk required 14 factors to decompose his reference spectra. He next had to select the number of independent variables needed to explain the composite spectrum and thus identify the constituents of the mixture that had generated the spectrum. He picked the number four, because he believed that only four things would influence the spectrum. These were the amounts of anhydrate and hemihydrate in the mixture, the amount of Nujol mull (a gel applied to the mixture to enable spectroscopic measurement) in it, and the mixture's thickness.

To determine whether a batch of anhydrate produced by Apotex contained 1 percent hemihydrate, Niemczyk created a reference sample consisting of anhydrate and hemihydrate in a ratio of 99 to 1, plus the Nujol mull; obtained the infrared spectrum of that sample; and then compared it (not by visual inspection but by means of the PLS formula) with the spectrum

of the test sample. If the spectra were identical, the comparison would show that the test sample contained 1 percent hemihydrate. He created other reference samples to test for other possible percentages of hemihydrate in the Apotex samples as well. He estimated intermediate percentages by extrapolation.

One of Apotex's expert witnesses, Dr. Peter Griffiths, contended that the number of degrees of freedom must equal the number of factors (minus one, but that is a technical detail that I can ignore). Niemczyk's analysis contained only four degrees of freedom, corresponding to the four independent variables that he identified, even though he used 14 factors. The significance of this point is that the more degrees of freedom employed in a PLS test, the more exacting are the criteria of statistical significance. To attain significance at a given level (such as 95 percent), the spectral F ratio must not exceed a specified level, and that level is lower the greater the number of degrees of freedom. Had Niemczyk used 14 degrees of freedom, the spectral F ratios that he obtained in his PLS tests of hemihydrate in Apotex's product would have been too high to be statistically significant.

Griffiths' criticism would be compelling if every factor (that is, every component of the reference spectrum) had to have a separate cause; then the need for 14 factors to decompose the spectrum would show that Niemczyk had failed to identify all the independent variables in play. As Niemczyk explained, however, if the spectral effect of a variable is nonlinear, several factors may be required to account for the nonlinearities, but the additional factors would not correspond to additional variables and so there would be no need to jack up the number of degrees of freedom and correspondingly lower the significance ceiling on the spectral F ratio.

Griffiths also questioned Niemczyk's method of determining the standard deviations of his estimates of the amount of hemihydrate contained in the Apotex samples that he examined. Suppose that the mean estimate of the percentage of hemihydrate in a sample were 5 percent with a standard deviation of 1 percent. Then the probability that the true value was between 3 percent and 7 percent, that is, within two stan-

dard deviations of the mean estimate, would be 95 percent, a standard measure of statistical significance. But if instead the standard deviation were 3 percent, the 95 percent confidence interval would run from –1 percent to +11 percent, and one would not be 95 percent sure that the sample in question actually contained a positive (>0%) amount of hemihydrate.

Dr. Griffiths was correct—the standard deviations computed by Dr. Niemczyk were too small, as Niemczyk essentially conceded when recalled to the stand after Griffiths testified—and as SmithKline essentially concedes, as well, in its post-trial brief. For there, instead of trying to defend Niemczyk's method, SmithKline states merely that, using Griffiths' method of computing the standard deviation, "Professor Niemczyk can still conclude with at least 80% to 85% confidence that five of nine of Defendants' batches contain measurable amounts of hemihydrate." This need not be a fatal concession, since 95 percent (i.e., a 5 percent probability that the sign of the coefficient being tested would be observed in the test even if the true value of the sign was zero) is an arbitrary measure of statistical significance. This is especially so when the burden of persuasion on an issue is the undemanding "preponderance" standard, which requires a confidence of only a mite over 50 percent. So recomputing Niemczyk's estimates as significant only at the 80 or 85 percent level need not be thought to invalidate his findings. But he did not recompute them, and so there is no evidence that his findings are significant at or even near those levels.

There are more problems with Niemczyk's evidence. SmithKline's lawyers gave him an anhydrate that SmithKline had created and dubbed "Form A"—had in fact patented (remember that SmithKline has patented various anhydrate crystals of paroxetine)—as well as the hemihydrate contained in Paxil, to be his reference samples. After Niemczyk created the reference samples and determined their spectra, the lawyers gave him batches of the bulk material that BCI ships to TorPharm for tableting. As we know, however, there are several anhydrate polymorphs of paroxetine besides Form A. There is of course Form 2, the anhydrate crystal before the hemihydrate

appeared. There are also Forms B, C, and D. All five of these polymorphs are manufactured by SmithKline. There is also a sixth polymorph of paroxetine, a solvate containing molecules of isopropyl alcohol (the solvent). There is also Form Z, which is what Apotex calls the anhydrate that it is manufacturing. Form Z appears to be either the same as, or very similar to, Form 2, which is what SmithKline was manufacturing before it switched to the hemihydrate. Of all the anhydrous forms of crystalline paroxetine hydrochloride, Form 2 is the one most likely to be within the public domain, so it is logical that Apotex's Form Z would track it closely.

All crystalline forms of paroxetine yield similar though not identical spectra, since all contain paroxetine molecules as their predominant component. That makes it important in a test for the presence of hemihydrate to be certain that the reference sample of anhydrate is of the same form as the anhydrate in the mixture to be tested, that is, in the Apotex samples. What is more, Apotex's samples contain impurities, each with its own spectrum signature. They are not the same impurities as in the reference samples, and spectra of different substances can be confusingly similar. An impurity in an Apotex sample could conceivably cause the sample's spectrum to be mistaken for the spectrum of a mixture containing hemihydrate.

What Niemczyk was doing, under the direction of the lawyers who had hired him, was comparing the spectrum of a mixture consisting of a 99:1 ratio of Form A anhydrate to hemihydrate (I need not discuss his other reference samples separately, which involve different ratios of Form A to hemihydrate), plus no doubt some impurities, with the spectrum of a mixture containing Apotex's Form Z ($\cong$ Form 2) anhydrate, other impurities, and—maybe—a small amount of hemihydrate. Maybe. An alternative possibility, however, is that the spectrum of Apotex's Form Z anhydrate mixture, when compared with the spectrum of the quite different mixture that Dr. Niemczyk was told was to be his reference sample (the Form A mixture supplied him by the lawyers), revealed differences that

were mistaken for proof that there was hemihydrate in the Apotex mixture.

Niemczyk had received another mixture from SmithKline, this one containing Form Z anhydrate manufactured by SmithKline. He had intended to determine its spectrum for possible use as a reference spectrum. It would have been the natural choice for a reference sample for a test of Apotex's mixture, which was also Form Z. But the lawyers told him not to test it, and he did not. Nor did they give him all the samples they had obtained of Apotex's product. Nor did they give him a variety of samples to test without telling him which were Apotex's. He knew what they wanted him to find, and he found it.

Was there *really* hemihydrate in Apotex's product in an amount detectable by the PLS method, or was Niemczyk's finding an artifact of the methodology that the lawyers imposed on him? My confidence in his testimony was shaken by the fact that his procedure had been manipulated by the lawyers—for reasons, by the way, that were never explained either to him or to me. I am particularly disturbed by their having forbidden him to test the Form Z sample as part of the process of creating reference samples. It was the one closest to Apotex's product and therefore the prime candidate to be the reference sample for a test of that product. I am also distressed by his failure to insist that they send him a variety of mixtures to test of which only one or a few would be Apotex mixtures. Moreover, as with any test, one wants the tester to be "blind." Dr. Niemczyk did not conduct a blindfold test of the Apotex samples.

I do not gainsay Niemczyk's claim, supported by most of the other witnesses, that every crystal generates a unique spectrum, just as every human being has, or so it is believed, a unique set of fingerprints. The question is the power of his methodology to discriminate among the different spectra generated by similar crystals. If you compared the sharp photograph of one person's fingerprints with a blurred photo of another person's fingerprints, you might conclude that they were the same person. The same kind of thing may well have happened here.

Dr. Batchelder is an expert in Raman microscopy, another recent but accepted method of determining the presence of small quantities of a given substance in a mixture. (Raman spectroscopy, as distinct from microscopy, is much older.) The Raman microscope plays a fine laser beam, only two microns in diameter (a micron is one one-thousandth of a millimeter), across the mixture, in effect sampling the particles that constitute the mixture. When the beam hits a particle, the particle scatters the beam in much the same way that a prism refracts light, producing (like the prism) a spectrum similar to that produced by infrared spectroscopy. Batchelder had to construct reference spectra and like Niemczyk he based these on an incomplete array of anhydrate forms (A, B, and C, but not D or Z, or the excipients used by Apotex—unlike Niemczyk, Batchelder was given pills to test, not the bulk material) furnished him by SmithKline's lawyers. With these spectra in hand he scanned samples of Apotex's anhydrate provided to him by SmithKline, hitting occasionally, according to Batchelder, crystals that generated the characteristic Raman spectrum of paroxetine hydrochloride hemihydrate. He got a higher reading when the laser was focused on the edge of the Apotex tablets, and he surmised that this was because in the last step of their production the tablets are sprayed with an aqueous coating. (His surmise was not admissible evidence, as he is not an expert in the manufacture of pharmaceuticals.) Although the average percentage of hemihydrate "hits" in the edge scans exceeded 8 percent, he explained that this figure could not be translated into an average weight of hemihydrate in Apotex's tablets. The edges are believed to contain more hemihydrate than the core of the tablets; more important, a percentage of Raman hits cannot be translated into a percentage of weight.

Apotex to the contrary notwithstanding, Raman microscopy is, potentially at least, a reliable method of determining the presence of hemihydrate in a mixture. The problem again lies with the lawyers' "feeding" of the expert. They gave Dr. Batchelder Apotex samples that were old and might have converted to hemihydrate under conditions not duplicated in BCI's and TorPharm's current production system. Further feeding

occurred when, because Dr. Batchelder had no experience in doing Raman microscopy on drugs, the leader of SmithKline's team of Raman microscopists, Dr. David Lee, instructed him in the preparation of a sample for a Raman scan—how and with what to slice the tablet, which tablets to scan, and what location on the tablets to scan.

Batchelder was aware of though not highly sensitive to the danger of conversion, and to reduce it he substituted epoxy resin for hot wax in preparing each sample for the microscope—but the pills were left in the open air while the epoxy was drying. And he performed his Raman tests on Apotex's pills in a SmithKline facility that is seeded with hemihydrate. SmithKline, which throughout the trial was constantly rounding on Apotex for failing to take this or that precaution to prevent anhydrate from being exposed to air during the manufacturing process, was remarkably indifferent to that danger when its experts were conducting the tests that it hoped would reveal the presence of hemihydrate. It's as if SmithKline's lawyers had asked Apotex's witnesses: "Why didn't you do what we didn't do?"

One of Dr. Batchelder's assistants, a Dr. Webster, in slicing Apotex's pills to prepare their contents for the microscope, used a nondisposable brush to wipe the blade after each slice. The brush was kept clean by "dusting," and so may have been infested with hemihydrate seeds that the brush transferred to the blade and thence to the mixture to be examined under the microscope. In addition, Webster's lab book states that he regularly brushed debris off the *pills* as well as off the blade. Batchelder testified that he didn't think Webster had actually brushed the pills; "I just think this is slightly sloppy writing within his lab book." I would be more impressed if Webster, the author, had testified about the entry in his lab book. He did not. And Batchelder did not comment on Webster's testimony that he had brushed the blade.

Dr. Lee and his team are highly experienced in conducting Raman tests of drug samples, including tests to determine the presence of paroxetine hydrochloride hemihydrate in a mixture. Yet SmithKline never asked Lee or his team to test Apo-

tex's samples for hemihydrate. (SmithKline refers for the first time in its post-trial brief, without citation, to a protective order that it claims forbade Lee to analyze Apotex's samples. When at the trial I asked Lee why he hadn't been the one to perform the tests, he said the lawyers had told him they needed an outside expert; that would have been lawyers' cue to mention the protective order, but they did not.) Instead he was directed to teach Batchelder how to do it. He told Batchelder to keep careful notes of the instruction and after completing it gave him a test to make sure he'd learned how to use Raman microscopy to determine the presence of paroxetine hydrochloride hemihydrate in an anhydrate mixture. In other words, the *real* expert was an employee of the defendant, and the nominal expert was a novice in testing mixtures for hemihydrate who had to be taught by the employee.

Whether because of inexperience or incomplete instructions, Batchelder omitted precautions that would have enhanced the reliability of his results. I have mentioned some of these omissions and here I add that given the possibility that the laser beam itself might cause conversion, he should probably have examined the same anhydrate crystal at intervals to see whether the crystal had altered its composition in the interim. There was an inconclusive back and forth at trial about whether the beam (which is not hot) could precipitate conversion; the issue could have been resolved long before trial, by proper experimentation by Dr. Batchelder—or Dr. Lee, the real expert on Raman microscopy of drug polymorphs.

Although Lee is an employee doubtless loyal to SmithKline, expert witnesses are not known for biting the hand that feeds them, here very generously. Dr. Batchelder has been paid almost $150,000 for his work in this case. (SmithKline has paid its testifying experts in this case almost $1 million; Apotex has paid its testifying experts more than $250,000.) I would have been more impressed by Lee's testifying to the result of his or his team's doing a Raman scan of the Apotex samples than I was by Batchelder's testimony. I was additionally troubled to learn that of the three Raman experts whom SmithKline considered for hiring to be an expert witness, the two who were

turned down in favor of Batchelder had extensive experience in Raman microscopy of drug compounds. Batchelder had virtually none, which is why he required a tutorial by Dr. Lee.

Although witness after witness testified to the importance of doing multiple tests on the same sample because of the potential for error and ambiguity in tests of crystal structure, no sample of Apotex's product was tested both by PLS-enhanced spectroscopy and Raman microscopy. Nor did Niemczyk or Batchelder test all the samples of Apotex product that SmithKline had obtained in discovery. Although I specifically asked SmithKline how many samples had been obtained from Apotex and how many of them had been tested by Niemczyk or Batchelder, I never received a satisfactory answer. As near as I can determine, Niemczyk tested 9 out of 52 samples of bulk material and Batchelder 16 out of 29 batches of pills. The pill batches, however, sometimes consisted of more than one bottle of pills and I have no idea how many pills in all were produced to SmithKline and why Batchelder singled out certain of them but not others for testing. Moreover, for unexplained reasons he did many more scans of some pills than of others. Also unexplained is why he did edge scans of some pills but not of others.

It was also never explained at trial why Niemczyk tested just bulk material and Batchelder just pills. In its post-trial brief, SmithKline, without record references, says that Niemczyk was given bulk material to test because his methodology was an excellent one for bulk material and had been used in a previous patent case of SmithKline's, involving a different drug, on bulk material, while Batchelder was given tablets because Raman microscope can do edges. Neither proposition, even if credited despite the absence of record support (as I am disinclined to do, for it was a question I had put to SmithKline early in the trial), suggests that Raman cannot be done effectively on bulk material or PLS effectively on tablets.

For all these reasons, taken together, I apply a sharp discount factor to both Niemczyk's and Batchelder's testimony. Indeed, I might well have been justified in excluding their testimony altogether under the standard of *Daubert v. Merrell*

Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993); see also Fed. R. Evid. 702, as urged by Apotex, on the ground that these two scientists did not do their work for SmithKline in this litigation with the same rigor with which they do their academic work. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999); *Sheehan v. Daily Racing Form, Inc.*, 104 F.3d 940, 942 (7th Cir. 1997); *Cummins v. Lyle Industries*, 93 F.3d 362, 369 (7th Cir. 1996). This by the way is another issue controlled by regional, not Federal Circuit, procedural law, *Micro Chemical, Inc. v. Lextron, Inc.*, 317 F.3d 1387, 1390–91 (Fed. Cir. 2003), though with respect to the *Daubert* issue the distinction is not important because Seventh Circuit law tracks the Supreme Court's authoritative pronouncements, as of course Federal Circuit law does as well.

The primary purpose of the *Daubert* filter is to protect juries from being bamboozled by technical evidence of dubious merit, *Seaboard Lumber Co. v. United States*, 308 F.3d 1283, 1301–02 (Fed. Cir. 2002), as is implicit in the courts' insistence that the *Daubert* inquiry performs a "gatekeeper" function. E.g., *Smith v. Ford Motor Co.*, 215 F.3d 713, 718 (7th Cir. 2000). In a bench trial it is an acceptable alternative to admit evidence of borderline admissibility and give it the (slight) weight to which it is entitled. The Federal Circuit in *Seaboard Lumber Co. v. United States, supra*, 308 F.3d at 1302, while pointing to the concern with protecting juries from confusion, did say that the *Daubert* standard must be followed in bench trials as well. But it did not say that it must be followed *rigidly* in such trials. *Daubert* requires a binary choice—admit or exclude—and a judge in a bench trial should have discretion to admit questionable technical evidence, though of course he must not give it more weight than it deserves. This at any rate was my approach with respect to Niemczyk and Batchelder, and I do not consider their evidence to have been wholly lacking in credibility or probative value. While the sum of zero plus zero is zero, the sum of one plus one is two; and the convergent result of two weak tests is more robust than the result of each test taken in isolation; so maybe one plus one is three. But if

proof by a preponderance of the evidence is modeled as scoring 5.01 points out of 10, then 3 out of 10 won't hack it.

This cannot conclude the analysis, because of the evidence discussed earlier concerning the tests that BCI conducted on its product, and because of testimony by Dr. Byrn that with proper methods Apotex could probably keep the amount of hemihydrate in its product down to the 2 to 4 percent range. The implication is that even if Niemczyk and Batchelder failed to detect hemihydrate, the methods they used could have done so; and just as existence and detection are not the same thing, neither are detectability and detection. Still, the unimpressive showing by Niemczyk and Batchelder, both skilled practitioners of their respective methods for detecting minute percentages of a polymorph in a mixture with another polymorph, leaves me highly skeptical. My doubts are enhanced by the profound scientific uncertainty concerning the mechanism and precise effects of adventitious seeding both in general and specifically with respect to paroxetine hydrochloride hemihydrate, by the fact that I am making a predictive judgment, and by the fact that the other evidence of conversion, designed to bolster Niemczyk and Batchelder, is, as I discussed earlier, very weak. Although I regard the question as a close one, I conclude that SmithKline has failed to prove by a preponderance of the evidence that Apotex is likely to produce a product that contains enough hemihydrate to be detectable even by PLS or Raman.

Only if the "single crystal" interpretation of claim 1 is correct, therefore, has SmithKline proved infringement. But if that interpretation is correct, the patent is invalid for indefiniteness.

Seeding as an Equitable Defense

But now suppose all this is wrong and SmithKline *has* proved infringement of a valid claim 1. It must still lose this case, for two independent reasons both rooted in equity. Equity figures in two fundamental ways in law. First, it is a source of defenses to liability—in patent as in other cases, as illustrated by the well-known defense of prosecution-history estoppel. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S.

722 (2002). Second, it furnishes the norms that guide the grant or denial of equitable relief. Both figure here. But before proceeding further I must emphasize that in referring to "equity" I am referring not to some vague sense of "fairness" but to the body of principles that has crystallized (pardon the pun) over centuries of Anglo-American jurisprudence and become a part of patent law as of the other fields of American law.

Although I cannot find any statutory language or case law that bears on the question, I believe that as a matter of fundamental principle it must be a defense to a charge of patent infringement that the patentee caused the infringement. There are many analogies, but one will suffice: it is a completely orthodox defense to a suit for breach of contract that the plaintiff prevented the defendant from performing his contractual duty. See, e.g., *Zobel & Dahl Construction v. Crotty*, 356 N.W.2d 42, 45 (Minn. 1984); *Pfaff v. Petrie*, 71 N.E.2d 345, 351 (Ill. 1947); *Chicago Title & Trust Co. v. Hedges Mfg. Co.*, 414 N.E.2d 232, 236–37 (Ill. App. 1980). Had SmithKline snuck into BCI's plant and scattered hemihydrate seeds, I do not think that even SmithKline would deny that Apotex would have a good defense to a claim of infringement of patent 723.

Of course, SmithKline did not do that. It did not deliberately seed BCI's plant. And no evidence was presented as to whether Apotex could have made the hemihydrate that it produced in the course of development of its anhydrous paroxetine product in some other facility, which would then no doubt become seeded but could be abandoned or diverted to another product and the anhydrate be produced at BCI's virginal facility. But would it remain virginal? Quite possibly not, since some of the personnel involved in the experimental preparations at the remote facility would have occasion to visit BCI and there would be no way to disinfect them of seeds before the visit. Remember ritonavir. Remember too that Apotex was within its rights in making hemihydrate for experimental purposes because the Hatch-Waxman Act allows manufacturers to experiment with a patented drug while developing its generic equivalent.

SmithKline urged repeatedly throughout the trial that while seeds are not necessary to produce paroxetine hydrochloride hemihydrate, they are necessary for the conversion of anhydrate to hemihydrate. If there are seeds in BCI's plant, how did they get there? There are only two possibilities consistent with the trial record. The first is that they wafted there from SmithKline. The second is that they were produced when Apotex made hemihydrate as part of its developmental process. That was not infringement; that was a licensed use, licensed by virtue of the Hatch-Waxman Act, of SmithKline's property right. The ultimate responsibility for the seeding of BCI's plant was SmithKline's.

SmithKline harped incessantly at the trial on the fact that Apotex applies an aqueous coating to its anhydrate pills rather than a nonaqueous coating, such as shellac. But the head of TorPharm (remember it is TorPharm that makes the pills out of the bulk material that it receives from BCI) testified without contradiction that the U.S. and Canadian regulatory authorities discourage the use of the nonaqueous coatings on pills. So it seems that on SmithKline's theory of infringement, between government and SmithKline generic producers are disabled from producing a public-domain product however strenuous the efforts they make to avoid committing a purely nominal infringement.

SmithKline goes so far as to argue that what prevented Apotex from manufacturing a stable anhydrate, that is, one that would not convert to hemihydrate if seeded, is that SmithKline had obtained a patent on the stable anhydrate (Form C). And this flags a more general concern. According to sources discussed in Bernstein, *supra*, at 9–10, the more money that is spent looking for polymorphs, the more polymorphs are found. As a result, the pharmaceutical industry sees more than its share of polymorph discoveries. We know from Ostwald's Rule that later-discovered polymorphs tend to be more stable than the earlier ones. Just as SmithKline argues that Apotex's anhydrate converts to hemihydrate, hemihydrate itself may convert to a new, more stable form of anhydrate discovered and patented by SmithKline, resulting in the indefinite extension of

what is in effect Ferrosan's discovery in the 1970s of paroxetine. Patent 723 will expire in three and a half years. But SmithKline's patent on Form C will not expire until 2016 at the earliest, 39 years after Ferrosan obtained patent 196.

To repeat an earlier point, Apotex gains nothing from the seeding of its plant. As Dr. Batchelder put it, if you are trying to make anhydrate, any hemihydrate that gets into it is an impurity. The effect of seeding is to impose on Apotex additional costs of production as it makes efforts, probably, as I have said, in vain, to purge its production process of hemihydrate seeds. Apotex is not appropriating value that belongs to SmithKline by virtue of patent 723, because it is incurring costs rather than reaping any benefits from the fact that BCI's plant is seeded and therefore some of its anhydrate may convert to hemihydrate. The only possible effect of preventing the alleged infringement would be to perpetuate an expired patent (patent 196, which expired more than a decade ago) by making it impossible for Apotex to manufacture a formerly patented substance that is now in the public domain. That would be true even if, to recur to an earlier example, Apotex had spent a billion dollars to purge BCI's plant of hemihydrate seeds. The purging would probably fail (remember that a seed might be as small as 10 molecules); and the expenditure on the attempt would have no social product and should not be encouraged.

The case for Apotex's having an affirmative defense to infringement is stronger the broader the interpretation of claim 1. Apotex has taken steps to avoid producing hemihydrate in amounts detectable under traditional measures with their 5 to 8 percent limit of detection, and SmithKline itself argues that by heroic means Apotex could even get below the limits of detection by PLS and Raman microscopy. But Apotex cannot eliminate *all* crystals of hemihydrate; under a single-crystal interpretation of claim 1, SmithKline is the sole cause of infringement.

Mention of equitable defenses to patent infringement brings to mind the Federal Circuit's statement of just two months ago concerning the reverse doctrine of equivalents, "under which an accused product or process that falls within

the literal words of a claim nevertheless may not infringe if the product or process 'is so far changed in principle from a patented article that it performs the same or a similar function in a substantially different way.' *Graver Tank & Mfg. Co. v. Linde Air Prod. Co.*, 339 U.S. 605, 608–09 (1950); see generally Donald S. Chisum, 5A *Chisum on Patents* § 18.04 (1999). This doctrine is equitably applied based upon underlying questions of fact, see *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1581 (Fed. Cir. 1991), when the accused infringer proves that, despite the asserted claims literally reading on the accused device, 'it has been so changed that it is no longer the same invention.' *Del Mar Avionics, Inc. v. Quinton Instr. Co.*, 836 F.2d 1320, 1325 (Fed. Cir. 1987) (citing *Graver Tank*, 339 U.S. at 608–09)." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1351 (Fed. Cir. 2003).

The defense failed in *Amgen*. The court was "not persuaded by TKT that this is a case where equity commands a determination of non-infringement despite its product literally falling within the scope of the asserted claims." *Id.* But what is more important is the court's recognition that there might be a case "where equity commands a determination of non-infringement despite its product literally falling within the scope of the asserted claims." This is a pretty good description of the present case, though since Apotex did not invoke the reverse doctrine of equivalents I do not rely on it. This is a case in which the patented product on which the claim of infringement is based has been so changed that it is no longer the same invention. The hemihydrate that is found in small quantities in the anhydrate is not the same invention covered by patent 723; it is merely an impurity.

Equitable Limitations on Patentee Relief

But suppose this too is wrong, and Apotex is guilty of infringement and has no defenses. The next and last question I need consider is relief. The relief sought by SmithKline, apart from attorney's fees on the ground that Apotex's infringement was willful, is twofold: an injunction against Apotex's producing the anhydrate until patent 723 expires and an order, au-

thorized by the Hatch-Waxman Act, in effect directing the FDA to delay its granting Apotex's ANDA until patent 723 expires, an order that would have the same effect as the injunction.

The grant of an injunction in the circumstances disclosed by the evidence in this case would be a travesty of equity. An injunction is a substitute for an award of damages in situations in which damages are difficult to calculate or are otherwise inadequate as a remedy for the wrong done by the defendant to the plaintiff. *Walgreen Co. v. Sara Creek Property Co., B.V.*, 966 F.2d 273, 274–76 (7th Cir. 1992); *Ocean Spray Cranberries, Inc. v. PepsiCo, Inc.*, 160 F.3d 58, 61 (1st Cir. 1998). It is not to provide relief when damages are known to be zero. To provide relief in such a case would be to invite a form of extortion. *Marseilles Hydro Power, LLC v. Marseilles Land & Water Co.*, 299 F.3d 643, 651 (7th Cir. 2002); *Youngs v. Old Ben Coal Co.*, 243 F.3d 387, 393 (7th Cir. 2001). A plaintiff who told a court that he wanted an injunction *because* he had not sustained and did not expect to sustain any damages whatsoever, but that naturally he wanted *something* to show for the bother of having sued and the something he wanted was an injunction that he could use to extract a licensing fee, would be thrown out of court on his ear. But consider what damages SmithKline might seek in the event that Apotex is permitted to produce and sell its anhydrate and the anhydrate is discovered to contain 2 percent (or perhaps 5 or even 10 percent—i.e., well short of "high double digits") hemihydrate. "Damages is the amount of loss to a patentee." *SmithKline Diagnostics, Inc. v. Helena Laboratories Corp.*, 926 F.2d 1161, 1164 (Fed. Cir. 1991). Since the hemihydrate in Apotex's product would not be replacing any hemihydrate sold by SmithKline or (until it reached the high double digits, which has not been proved to be likely) doing anything for Apotex that might give it a competitive advantage that would inflict a loss on SmithKline, SmithKline would have no lost profits; its damages would be zero.

Against this SmithKline argues that it would suffer a loss measured by the diminution in its profits from Paxil as a result of competition from Apotex's anhydrate, which has the same therapeutic benefit as Paxil. But a patentee will not be heard

to complain of losses that are due to competition from a product that is in the public domain. (Of course I am assuming as I must that Apotex won't be infringing an anhydrate patent of SmithKline's; that is the issue in other litigation.) The implication of such a complaint would be that patents should last forever and generic equivalents be outlawed. The engine of the competition that SmithKline fears is not the 2 or 5 or 10 percent hemihydrate in Apotex's product, if that is what there is going to be, but the 98 or 95 or 90 percent anhydrate; for Apotex's competition would not be less effective if the product were 100 percent anhydrate.

Another way to explain SmithKline's disentitlement to an injunction is in terms of the doctrine, classically equitable—an aspect of the historic doctrine of "unclean hands"—of patent misuse. *C.R. Bard, Inc. v. M3 Systems, Inc., supra,* 157 F.3d at 1372. The core of that doctrine is the proposition that a patent may not be used to obtain more protection from competition than patent law contemplates. The doctrine is defined in and illustrated by *Morton Salt Co. v. G.S. Suppiger Co.*, 314 U.S. 488, 491–93 (1942), where we read that "the use of [a patent] to suppress competition in the sale of an unpatented article may deprive the patentee of the aid of a court of equity to restrain an alleged infringement by one who is a competitor." *Id.* at 491. The patentee of a machine for processing salt required its customers to buy the salt for use in the machine from the patentee as well. This was held to be patent misuse. The example is archaic and the outcome wrong (and now largely superseded, see 35 U.S.C. § 271(d)(5)), because "tying" an unpatented to a patented product is not, as was believed when *Morton Salt* was decided, an effective method of extending the patent monopoly. Cf. *In re Independent Service Organizations Antitrust Litigation*, 203 F.3d 1322, 1326–27 (Fed. Cir. 2000). The machine and the salt were complements, in the economic sense that two products are complements if an increase in the price of one causes a reduction in the demand for the other. If the patentee refused to license its machine unless the licensee paid him a monopoly price for the salt that he needed if he was to obtain any benefit from using the machine, the patentee could not

charge as much for the license. See, e.g., *Scheiber v. Dolby Laboratories, Inc.*, 293 F.3d 1014 (7th Cir. 2002).

The present case illustrates, in contrast to *Morton Salt* and other tying cases, the economically *rational* use of a patent to obtain patent protection beyond the contemplation of patent law. Cf. *Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1581 (Fed. Cir. 1991) ("double patenting" doctrine). SmithKline owned a patent on anhydrous paroxetine that expired in 1992. At that point anhydrous paroxetine entered the public domain and any firm that could satisfy the FDA that its anhydrate was bioequivalent to SmithKline's hemihydrate approved by the FDA that year for sale to the public could compete with SmithKline as soon as the FDA's five-year embargo on the sale of a bioequivalent of a new chemical entity ended. (It was only later that SmithKline muddied the waters by obtaining additional paroxetine patents.) Were SmithKline to obtain an injunction against Apotex's producing and selling its anhydrous Paxil substitute, it would be as if the original patent, 196, had not expired in 1992 but instead will not expire until 2006. SmithKline will have gained a 14-year extension of the patent term without authorization in the patent statute. Maybe the statutory term of drug patents is too short, as SmithKline argued in one of its filings in this case, but that is a complaint to be made to Congress rather than to the courts.

By no means do I advocate making "patent misuse" a general equity solvent for "sympathetic" cases. See *C.R. Bard, Inc. v. M3 Systems, Inc.*, *supra*, 157 F.3d at 1373. I have written against that misuse of misuse, *USM Corp. v. SPS Technologies, Inc.*, 694 F.2d 505, 510–12 (7th Cir. 1982), as have the Supreme Court and other courts against parallel proposals to subordinate bankruptcy law to vague equitable standards. *Butner v. United States*, 440 U.S. 48, 55–56 (1979); *In re Stoecker*, 179 F.3d 546, 551 (7th Cir. 1999); *In re Ludlow Hospital Society, Inc.*, 124 F.3d 22, 27 (1st Cir. 1997). It does not follow that patent misuse is a closed category. When the advance of science well illustrated by the products in this case enables a form of patent misuse that is new but is well within the conceptual heartland of the doctrine, the boundaries of the

doctrine can expand modestly to encompass it. "The sea-changes in both law and technology stand as a testament to the ability of law to adapt to new and innovative concepts, while remaining true to basic principles." *AT&T Corp. v. Excel Communications, Inc.*, 172 F.3d 1352, 1356 (Fed. Cir. 1999). It would be inappropriate to confine patent misuse, as is sometimes suggested, to practices that violate antitrust law, for in that event the doctrine would be superfluous.

But mention of antitrust serves to bring to mind the close analogy between the form of patent misuse that I am exploring and the doctrine of "antitrust injury." *Brunswick Corp. v. Pueblo Bowl-O-Mat, Inc.*, 429 U.S. 477, 486–88 (1977); *Atlantic Richfield Co. v. USA Petroleum Co.*, 495 U.S. 328, 337, 339 (1990); *Dial A Car, Inc. v. Transportation, Inc.*, 82 F.3d 484, 486–87 (D.C. Cir. 1996). Suppose that two competing firms merge in violation of antitrust law, but so efficient is the merger that the effect of eliminating competition between the merging firms on the market price (maybe they have so large a share of the market that jointly they enjoy a practical monopoly) is dominated by the effect of the merger in reducing the costs of the firm resulting from the merger, compared to the costs of the predecessor firms; and in consequence the firm reduces its price below the old competitive price. This is not a fanciful example; if a monopolist's costs are much lower than those of the competitive industry that it has replaced, it is entirely possible that the optimal monopoly price will lie below the former competitive price. The remaining firms in the market must now lower their price in order to remain competitive, and so they are injured. But the injury is not actionable, as *Brunswick* and subsequent cases make clear. It is not "antitrust injury" (that is, injury for which antitrust law provides a remedy) because it is not the sort of injury that antitrust seeks to remedy.

Likewise any injury that SmithKline sustains from the fact that minute amounts of its product creep into Apotex's generic product will be due not to the invasion of any interest that patent law protects, but merely to the fact that the existence of a public-domain substitute for a patented product injures the

patentee by providing competition. Again, at the risk of tedious repetition, the efficacy of Apotex's generic competition with Paxil will gain nothing from the fact that Apotex cannot eliminate minuscule quantities of the hemihydrate from its anhydrate product. The infiltration of Apotex's production process by hemihydrate is merely a pretext for an infringement suit designed to prevent competition from a product that is in the public domain. It is like the complaint of the fringe firms in my merger example about having to compete with a firm that has lower costs.

The doctrine of antitrust injury is not esoteric but instead illustrates the general principle that causation in the legal sense requires that the injury to the plaintiff be the kind of injury that the law that the defendant violated was intended to prevent. The principle is illustrated by the colorful though very sad old case of *Gorris v. Scott*, 9 L.R.-Ex. 125 (1874). The plaintiff's animals, while being transported on the deck of defendant's ship, lost their footing and were swept overboard in a storm. The ship was not equipped with pens required by statute to prevent the spread of disease among the animals. Had there been pens, the animals would not have been washed overboard. But the plaintiff lost the case because the statute was not aimed at preventing that type of injury. See *Jack Walters & Sons Corp. v. Morton Bldg., Inc.*, 737 F.2d 698, 708–09 (7th Cir. 1984); W. Page Keeton *et al.*, *Prosser & Keeton on the Law of Torts*, § 36, pp. 222–26 (5th ed. 1984). The principle is general and I cannot think of any reason why it should not apply to patent law, although I have found only one opinion that endorses the principle, and that a dissent, *Rite-Hite Corp. v. Kelley Co.*, 56 F.3d 1538, 1558–60, 1575 (Fed. Cir. 1995) (en banc)—but the majority did not reject (or endorse) the principle.

SmithKline acknowledges as it must the applicability of equitable principles to the grant of injunctions in patent cases, 35 U.S.C. § 283; *Rite-Hite Corp. v. Kelley Co., Inc.*, *supra*, 56 F.3d at 1547–48, and complains about their application to its request for an injunction (should I find as I have that it has failed to prove that Apotex's product will contain more than in-

finitesimal amounts of the hemihydrate) only on the inadmissible ground that Congress has not made the statutory term of drug patents long enough. But it denies that the alternative remedy that it seeks under the Hatch-Waxman Act is subject to equitable principles. The principal argument that it makes in support of this distinction (which it actually forgot in a portion of its post-trial brief in which it stated that in the case of "single crystal" infringement "it would be unlikely that a court would grant injunctive relief *or anything* other than nominal damages" (emphasis added)) is that the erasure of equitable principles was part of the quid pro quo for the right of experimental use that the Act granted the generic manufacturers.

I am troubled not by the novelty of the argument but by the lack of evidence to support it. The patentee's quid for the generic manufacturer's quo in the Hatch-Waxman Act was the extension of the patent term while the patentee was seeking the FDA's approval to market the patented drug, 35 U.S.C. § 156(c), plus the mandatory 30-month stay of FDA approval if the patentee sued a generic manufacturer for infringement. 21 U.S.C. § 355(j)(5)(B)(iii). See, e.g., *Warner-Lambert Co. v. Apotex Corp.*, *supra*, 316 F.3d at 1357; H.R. Rep. No. 857 (Part I), 98th Cong., 2d Sess. 14–15 (1984); H.R. Rep. No. 857 (Part II), 98th Cong., 2d Sess. 11 (1984); Kristin E. Behrendt, "The Hatch-Waxman Act: Balancing Competing Interests or Survival of the Fittest?" 57 *Food & Drug L.J.* 247, 270 (2002). If the kind of hypertechnical infringement involved in this case (assuming that there is infringement at all, which I have found there is not) does not justify the issuance of an injunction—if indeed such issuance would ratify patent misuse directed against the manufacturers of generic drugs—what sense would it make to hold that the Hatch-Waxman Act, the main purpose of which was to facilitate competition from those manufacturers, entitles the patentee to precisely that inequitable remedy? It would make no sense. It would be a judicial amendment motivated by sympathy for SmithKline's argument that the patent term is too short for drugs. The Federal Circuit has held that in a case governed by the Hatch-Waxman Act "the substantive determination whether actual infringement or in-

ducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits, including those in a non-ANDA context, the *only* difference being that the inquiries now are hypothetical because the allegedly infringing product has not yet been marketed." *Warner-Lambert Co. v. Apotex Corp., supra,* 316 F.3d at 1365–66 (emphasis added). Under "traditional patent infringement analysis," SmithKline is not entitled to an injunction; so neither is it entitled to an order forbidding the FDA to approve Apotex's ANDA.

I am mindful that the Act uses "shall" rather than "may" language in reference to postponing the entry of the generic drug into the market, 35 U.S.C. § 271(e)(4)(A) ("the court shall order the effective date of any approval of the drug...involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed"), whereas the patent statute states that "courts having jurisdiction of cases under this title may grant injunctions in accordance with the principles of equity." 35 U.S.C. § 283. But "shall versus may" arguments are weak in general and in this case. As the Supreme Court noted in *Gutierrez de Martinez v. Lamagno,* 515 U.S. 417, 432 n. 9 (1995), "Though 'shall' generally means 'must,' legal writers sometimes use, or misuse, 'shall' to mean 'should,' 'will,' or even 'may.' See D. Mellinkoff, *Mellinkoff's Dictionary of American Legal Usage* 402–403 (1992) ('shall' and 'may' are 'frequently treated as synonyms' and their meaning depends on context); B. Garner, *Dictionary of Modern Legal Usage* 939 (2d ed. 1995) ('[C]ourts in virtually every English-speaking jurisdiction have held—by necessity that—*shall* means *may* in some contexts, and vice versa.'). For example, certain of the Federal Rules use the word 'shall' to authorize, but not to require, judicial action. See, e.g., Fed. Rule Civ. Proc. 16(e) ('The order following a final pretrial conference *shall* be modified only to prevent manifest injustice.') (emphasis added); Fed. Rule Crim. Proc. 11(b) (A *nolo contendere* plea '*shall* be accepted by the court only after due consideration of the views of the parties and the interest of the public in the effective administration of justice.') (emphasis added)." See also *Gray-Bey v. United States,* 201 F.3d 866, 867–

See also *Gray-Bey v. United States*, 201 F.3d 866, 867–70 (7th Cir. 2000).

In this case the natural explanation for the different usages has nothing to do with quids or quos. In the ordinary case of patent infringement, the infringement has already occurred and so damages are a possible remedy, and in deciding whether to grant an injunction the judge must weigh the pros and cons of the alternatives in the setting of the particular case. But the Hatch-Waxman order comes before any actual infringement, so there is no possible alternative remedy of damages (there is the possibility of an injunction against the infringer to back up the delay order, and that is authorized by section 271(e)(4)(B)). Section § 271(e)(4)(C) is explicit that the court may not award damages unless the infringer has begun commercial production or importation, that is, has begun competing with and therefore inflicting losses on the patentee, and so there cannot be a damages award in a case such as the present one. In a case such as this it is the order or nothing. The only relief possible is equitable. If equity requires in such an unusual case that the equitable relief sought be nothing, I cannot think of any reason for casting equity aside.

So the Supreme Court held in another "shall" case, *Hecht Co. v. Bowles*, 321 U.S. 321 (1944). The Emergency Price Control Act of 1942 provided that if the administrator of the Act showed that a person had violated it, an injunction or other order "shall be granted" by the court to which the administrator applied for relief. Yet the Court held that the court retained discretion to withhold relief in an appropriate case. A similar case is *Robbins v. McNicholas Transportation Co.*, 819 F.2d 682, 684–86 (7th Cir. 1987). The present case is stronger than either of these for softening the imperative force of "shall." Had Congress said "the court *may* order the effective date of any approval of the drug...involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed," it would have caused a good deal of judicial head-scratching. Judges would have wondered what on earth Congress had been thinking of when it said "may" rather than "shall." It could not have been thinking

about this case, unforeseen in 1984. I am not aware of any case before the present one in which the judge would have been warranted in withholding the delay order after finding infringement. Congress has neither the leisure nor the foresight (it would have to be omniscient) to provide an answer for every question that might arise in a case governed by one of its statutes. It enacts statutes against a background of legal understandings that inform the decision of unforeseen cases, and that include the principles of equity. Section 271(e)(4)(A) is an amendment to the patent statute and it provides relief in the nature of an injunction, for an injunction is simply a court order (other than a purely procedural one) to do or not to do something. As a form of patent injunction, the delay order is subject to the principles that govern such injunctions, although only in a very unusual case will those principles counsel for withholding relief. But this is the unusual case.

There is still another consideration. If Congress had wanted to extinguish judicial discretion to withhold the order postponing the entry of the generic drug, it could have done so very easily by providing not that "*the court shall order* the effective date of any approval of the drug...involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed" but instead that "the effective date of any approval of the drug...involved in the infringement *shall be* a date which is not earlier than the date of the expiration of the patent which has been infringed." Congress did not do that. That would have been like a law which says that a felon can't vote. The court decides whether the defendant committed a felony, but if it decides that he did, then the disqualification (corresponding to the postponement of the entry of the generic drug into the market) attaches automatically, without judicial intermediation. But here, instead of attaching a disqualification or other sanction automatically to an adjudicated infringer, Congress interposed the court between the statute and its application in an individual case by requiring that the order come from the court. No purpose would be served by such interposition if the court could never, no matter what the circumstances—however remote from any-

thing contemplated by Congress—refuse to issue the order once infringement had been established.

So SmithKline is entitled to no relief—but not because if there was infringement it was *de minimis*. Whether there is a *de minimis* defense in patent law is an unsettled question. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1565–66 and n. 1 (Fed. Cir. 1997). Clearly there is no such defense in general, because that would amount to a license to steal. E.g., *Pile v. Pedrick*, 31 Atl. 646 (Pa. 1895). That is why the defense is rejected in cases that involve intentional torts, such as conversion. *Hessel v. O'Hearn*, 977 F.2d 299, 303–04 (7th Cir. 1992). Patent infringement can be inadvertent as well as deliberate, as this case dramatically illustrates, but often it is deliberate and in such cases a *de minimis* defense would be unsound. The fair use defense of copyright law has a *de minimis* component, as where a writer copies a brief passage from a copyrighted work, but the reason is that since the brief passage is not a substitute for the copyrighted work but if anything an advertisement for it, the copyright holder could be expected to grant a license without demanding a fee, if a transaction were feasible, which it is not because of the stakes are so trivial. *Ty, Inc. v. Publications Int'l Ltd.*, 292 F.3d 512, 517–18 (7th Cir. 2002).

The reason for excusing the alleged infringement in this case is not that Apotex stole only a little hemihydrate from SmithKline. It stole nothing from SmithKline. It doesn't *want* hemihydrate, and it derives no value from the hemihydrate that it unavoidably creates and "sells." If it made hemihydrate deliberately, or if it took advantage of 100 percent conversion to obtain a product that had hemihydrate's superior handling characteristics, that would be theft and it would be nonsense to point out that paroxetine is only 10 percent of the pill by weight. But if the person sitting next to me at dinner spills his soup on my sleeve, I am not a thief even though I cannot remove the stain.

The distinction between the present case and a "pure" *de minimis* case is made clear in Judge Learned Hand's opinion in *Condenser Corp. v. Micamold Radio Corp.*, 145 F.2d 878, 880

(2d Cir. 1944) (citations omitted), where he said that "we will not enjoin the defendant's machine for a detail, obviously so useless in function. Moreover, it would be equally unwarranted to give judgment for damages or profits; for it is inconceivable that the infringement, if there is any at all,...could add a cent to the defendant's profits, or could interfere in the slightest degree with the plaintiff's sales." See also *Pratt v. United States*, 43 F. Supp. 461, 475–76 (Ct. Cl. 1942). Cf. *Kaz Mfg. Co. v. Chesebrough-Ponds, Inc.*, 317 F.2d 679, 680–81 (2d Cir. 1963): "one who constructs a patented wall safe but uses it only as an anchor for his boat would not be a patent infringer since such use would not be for the purpose of utilizing the teachings of the patent." *Id.* at n. 3.

SmithKline points out that Apotex wants to take a free ride ("usurping," SmithKline calls it) on the considerable investment made by SmithKline in obtaining FDA approval for Paxil. It is indeed much easier to establish bioequivalence than it is to convince the FDA that an original drug is safe and effective. But that kind of free riding the law permits, and indeed the Hatch-Waxman Act encourages. Moreover, free riding is an integral part of the scheme of the patent law. In exchange for the exclusive and in the case of Paxil very valuable rights that a valid patent grants, the patentee is required to make public disclosure of the steps required to create the patented product, so that when the patent expires and the patented product enters the public domain competitors can manufacture the product. Those competitors are free riders with a vengeance. But they are lawful free riders. And so is Apotex.

To summarize:

I construe claim 1 of SmithKline's patent 723 to cover crystalline paroxetine hydrochloride hemihydrate in any commercially significant quantity, and so construed the claim is valid against the various attacks on it made by Apotex but clearly will not be infringed by Apotex's anhydrate product. I hold that if claim 1 is construed to claim single crystals of crystalline paroxetine hydrochloride hemihydrate, it is infringed, but that

if the claim were so construed it would be invalid because of indefiniteness.

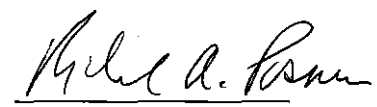
If claim 1 is construed to claim crystalline paroxetine hydrochloride hemihydrate in amounts detectable by means that existed when the patent was applied for or issued, I find that SmithKline has failed to prove by a preponderance of the evidence that Apotex's product will infringe claim 1.

I reach the same conclusion (though with less confidence) if claim 1 is construed to claim crystalline paroxetine hydrochloride hemihydrate in amounts detectable by any means. So construed, the claim might fail for indefiniteness, but I do not reach that question.

If contrary to the above, claim 1 is valid and will be infringed either by a single crystal of hemihydrate or by a barely detectable amount of it, Apotex has a complete affirmative defense that SmithKline is the cause of the infringement.

If claim 1 is valid and will be infringed and Apotex has no defense to liability, I hold that SmithKline nevertheless is entitled to no relief: neither an injunction against Apotex's making its anhydrate product nor an order based on the Hatch-Waxman Act delaying Apotex's sale of its anhydrate product until patent 723 expires. The grant of injunctive relief, whether under the patent statute or under the Hatch-Waxman Act, would be contrary to the principles of equity. SmithKline acknowledges the application of those principles to its request for an injunction, and I hold that they also apply to its request for the delay order that would have the identical effect as the injunction.

For these reasons I am instructing the clerk of the district court to enter a final judgment for the defendants, dismissing SmithKline's suit with prejudice.



Richard A. Posner
U.S. Circuit Judge

March 3, 2003