United States Court of Appeals for the Federal Circuit

BOSTON SCIENTIFIC CORPORATION AND BOSTON SCIENTIFIC SCIMED, INC.,
Plaintiffs-Appellees,

v.

JOHNSON & JOHNSON (ALSO KNOWN AS JOHNSON & JOHNSON, INC.), CORDIS CORPORATION, AND WYETH,
Defendants-Appellants.

2010-1230, -1231, -1233, -1234

Appeals from the United States District Court for the District of Delaware in consolidated case nos. 07-CV-0333, 07-CV-0348, 07-CV-0409, and 07-CV-0765, Judge Sue L. Robinson.

Decided: June 7, 2011

MATTHEW M. WOLF, Arnold & Porter LLP, of Washington, DC, argued for plaintiffs-appellees. With him on the brief were EDWARD HAN and JOHN E. NILSSON.

DAVID T. PRITIKIN, Sidley Austin LLP, of Chicago, Illinois, argued for defendants-appellants. With him on the brief were CONSTANTINE L. TRELA, JR., WILLIAM H.

BAUMGARTNER, JR., RUSSELL E. CASS and JUSTIN B. WEINER.

SANDRA A. FRANTZEN, McAndrews, Held & Malloy, Ltd., of Chicago, Illinois for amicus curiae Abbott Cardiovascular Systems Inc. With her on the brief were EDWARD A. MAS, II, STEPHANIE F. SAMZ and KATHLEEN A. DORTON.

Before BRYSON, GAJARSA, and MOORE, *Circuit Judges*.

Opinion for the court filed by *Circuit Judge* MOORE.
Circuit Judge GAJARSA concurs-in-part.

MOORE, *Circuit Judge*.

Johnson & Johnson, Inc. (J&J), Cordis Corp. (Cordis) and Wyeth (collectively, Appellants) appeal the decision of the United States District Court for the District of Delaware granting summary judgment that certain claims of U.S. Patent Nos. 7,217,286 (the '7286 patent), 7,223,286 (the '3286 patent), 7,229,473 (the '473 patent), and 7,300,662 (the '662 patent) (collectively, the patents-in-suit) are invalid for failure to comply with 35 U.S.C. § 112, ¶ 1. *Boston Scientific Corp. v. Johnson & Johnson, Inc.*, 679 F. Supp. 2d 539 (D. Del. 2010). The district court determined that the asserted claims of the '7286 patent, the '3286 patent, and the '473 patent (collectively, the 1997 patents) are invalid for lack of adequate written description and lack of enablement, and that the asserted claims of the '662 patent are invalid for lack of adequate written description. Because no finder of fact could reasonably determine that the asserted claims of the patents-in-suit contained an adequate written description, we affirm.

BACKGROUND

I. Drug-Eluting Stents

The patents-in-suit relate to drug-eluting coronary stents used in the treatment of coronary artery disease. Coronary artery disease is caused, in part, by atherosclerosis, a build-up of arterial plaque. Atherosclerosis limits the flow of blood and oxygen to the heart and can result in chest pain, blood clots, heart attacks, and other ailments.

In 1977, physicians first used a procedure called balloon angioplasty to reopen arteries closing because of atherosclerosis. During the procedure, the physician inserts a balloon catheter into an artery near the patient's groin and threads the catheter through the artery to the site of the blockage. The physician then inflates the balloon to reopen the narrowed artery. In many balloon angioplasty patients, the opened artery narrows again – a process known as restenosis. One of the key components of restenosis is a phenomenon called neointimal proliferation, wherein the smooth muscle cells of the artery multiply over time in response to injury caused by the inflation of the balloon. The result of neointimal proliferation is the renarrowing of the artery.

In the 1980s, physicians began using bare metal coronary stents to support the artery after the physician deflates the balloon. Although these bare metal coronary stents prevented the collapse of the artery and constriction due to scarring, restenosis remained a problem because the bare metal stents did not prevent neointimal proliferation.

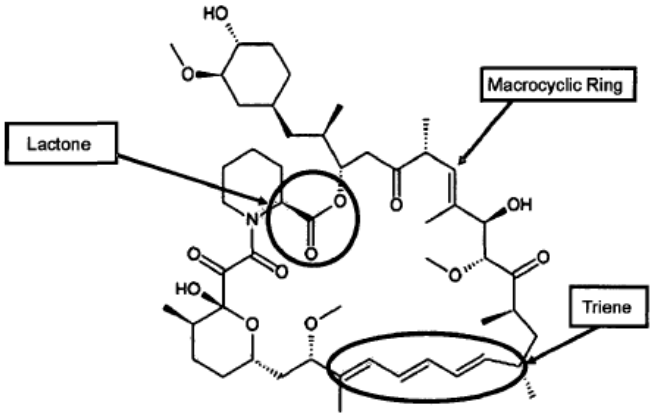
Researchers turned to a myriad of techniques in an attempt to prevent restenosis following balloon angioplasty. For example, researchers tested numerous oral drugs for the treatment of restenosis. J.A. 14732-39. One

of Appellants' experts characterized the number and variety of drugs tested as "reflect[ing] the lack of any clear path or direction toward a particular drug therapy for restenosis." J.A. 14732. Researchers also experimented with drug-eluting stents in an effort to prevent restenosis. Researchers believed that the drugs contained on such stents could help prevent neointimal proliferation. Cordis's Cypher® stent was the first drug-eluting stent approved by the United States Food and Drug Administration (FDA) and sold in the United States.

II. The Patents-In-Suit

The 1997 patents claim drug-eluting stents using either rapamycin or a macrocyclic lactone analog of rapamycin as the therapeutic agent. The '662 patent claims drug-eluting stents using either rapamycin or a macrocyclic triene analog of rapamycin.[1] The rapamycin molecule has a number of structural features including lactone and triene moieties. Thus, rapamycin is both a macrocyclic triene and a macrocyclic lactone. Rapamycin is depicted below with the macrocyclic ring, the lactone group, and the triene group identified:

[1] Under the district court's construction of the terms "macrocyclic lactone analog" and "macrocyclic triene analog," an analog of rapamycin is broadly defined as any molecule with structural similarity to rapamycin. *See Boston Scientific Corp. v. Johnson & Johnson, Inc.*, Civ. Nos. 07-333, 07-348, 07-409, 07-765-SLR, 2010 WL 331764, *2 (D. Del. Jan. 20, 2010) (Markman). The parties do not appeal the district court's claim construction ruling.



Appellees' Br. 10.

Cordis's Cypher® drug-eluting stent utilizes rapamycin as a therapeutic ingredient. Rapamycin (also called sirolimus) is a naturally occurring compound produced by the bacterium *Streptomyces hygroscopicus*. Scientists at Ayerst Research Laboratories (which later became part of Wyeth) isolated rapamycin, and the compound was first publicly described in articles published in 1975.

Researchers first investigated rapamycin as a potential antifungal. Later, researchers discovered that rapamycin exhibited other properties, including anti-tumor activity and immunosuppressant activity. In the early 1990s, researchers at Stanford University discovered that rapamycin inhibited restenosis after oral administration to rats.

Prior to the filing of the 1997 patents, some analogs of rapamycin were disclosed in the prior art. For example, PCT application WO 94/09010 (the Cottens publication) describes "novel alkylated derivatives of rapamycin having pharmaceutical utility, especially as immunosuppressants." J.A. 11059-11100. The Cottens publication specifically describes twenty-eight "preferred novel com-

pounds," twenty-five of which contain the same macrocyclic ring as rapamycin. J.A. 11063-64. These preferred analogs include everolimus. Everolimus is made by modifying rapamycin at a single location and is both a macrocyclic lactone and triene analog of rapamycin. *Boston Scientific Corp.*, 679 F. Supp. 2d at 543 n.3. Similarly, U.S. Patent No. 5,362,718 (the Skotnicki patent) claims and describes macrocyclic analogs of rapamycin and provides examples of fourteen specific structures. J.A. 10595-608.

A. The 1997 Patents

The '7286 patent, the '3286 patent and the '473 patent all descend from a provisional application filed in April 1997. The 1997 patents share a common specification and generally claim drug-eluting stents utilizing "rapamycin, or a macrocyclic lactone analog thereof" as the therapeutic agent. Cordis first added the phrase "macrocyclic lactone analog" to the claims during an April 7, 2006 claim amendment during prosecution of the '3286 patent. J.A. 20328-36. Cordis added these claims shortly after a competitor, Guidant, received European approval to sell a drug-eluting stent containing everolimus.

The 1997 patents' "Summary of the Invention" describes "[a] stent designed to include reservoirs . . . [,] a new approach which offers several important advantages over existing technologies." '7286 patent col.3 ll.43-45. The "Summary of the Invention" does not mention any particular therapeutic agent or any particular polymer coatings. The shared specification discloses that the reservoirs could be loaded with drugs and "[a] coating or membrane of biocompatible material could be applied over the reservoirs [to] control the diffusion of the drug from the reservoirs to the artery wall." *Id.* col.3 ll.61-65.

Later, in the "Detailed Description of Illustrative Embodiments," the shared specification discusses rapamycin for the first time. The specification identifies rapamycin as one of the "[n]umerous agents [that] are being actively studied as antiproliferative agents for use in restenosis and [that] have shown some activity in experimental animal models." *Id.* col.5 ll.8-10, 33. The 1997 patents indicate that rapamycin is of particular interest because it "is capable of inhibiting both the inflammatory response known to occur after arterial injury and stent implantation, as well as the [smooth muscle cell] hyperproliferative response." *Id.* col.5 ll.47-51. However, the specification also states that "the precise mechanism of rapamycin is still under active investigation," *id.* col.5 ll.36-38, and that "the ideal agent for restenosis has not yet been identified," *id.* col.5 ll.59-60.

The specification of the 1997 patents contains only a single reference to the claimed macrocyclic lactones. Under a subheading "Experiments," the specification states, "Agents: Rapamycin (sirolimus) structural analogs (macrocyclic lactones) and inhibitors of cell-cycle progression." *Id.* col.6 ll.4-5. The experiments disclosed under this subheading, however, only use rapamycin. The specification does not include any experiments using a macrocyclic lactone analog or even provide a single example of a macrocyclic lactone analog.

B. The '662 Patent

Cordis filed the application that issued as the '662 patent in 2004, but asserts that the claims are entitled to an effective filing date of January 25, 2001. The '662 patent defines rapamycin broadly to include "rapamycin, rapamycin analogs, derivatives and congeners that bind FKBP12 and possess the same pharmacologic properties as rapamycin." *See, e.g.*, '662 patent col.5 ll.48-51. The

'662 patent, like the 1997 patents, does not identify any specific species of rapamycin analogs.

Furthermore, the '662 patent does not identify what constitutes the claimed "macrocyclic triene analogs" of rapamycin, and provides no examples of "macrocyclic triene analogs." In fact, the only time the term "macrocyclic triene" is used in the specification is the brief statement that "[r]apamycin is a macroyclic [sic] triene antibiotic." *Id.* col.5 l.31. Unlike the 1997 patents where the shared specification mentions the genus (macrocyclic lactone analogs of rapamycin) and claims it in combination with other elements, here the inventors disclosed a genus (analogs of rapamycin), but claimed a narrower sub-genus of analogs (macrocyclic triene analogs of rapamycin) in combination with other elements. All of the data in the '662 patent relate to studies done with rapamycin coated stents — there is no data on stents using any rapamycin analog. As with the 1997 patents, Cordis added claim language specifying "macrocyclic triene analogs" only after Guidant received approval for an everolimus coated stent.

III. District Court Proceedings

Appellees Boston Scientific Corporation and Boston Scientific Scimed, Inc. (collectively, BSC), filed four complaints (later consolidated) against J&J and Cordis seeking declaratory judgments that the claims of the four patents-in-suit are invalid. *Boston Scientific Corp.*, 679 F. Supp. 2d at 542. BSC sells the accused Promus® Everolimus-Eluting Coronary Stent System (the Promus stent), which uses everolimus to prevent restenosis following implantation. *Id.* at 543. The Promus stent is BSC's private labeled version of Abbott Cardiovascular Systems Inc.'s (Abbott) XIENCE V® Everolimus-Eluting Coronary Stent System. *Id.* Appellants previously asserted the

patents-in-suit against Abbott in four civil actions in the District of New Jersey. *Id.* at 542.

In this action, the Appellants counterclaimed for infringement. *Id.* at 542. Wyeth, as a co-owner of the '662 patent with Cordis, is a party to the action involving the '662 patent. *Id.* at n.1.

The parties filed several summary judgment motions with the district court regarding validity and infringement. *Id.* at 542. Relevant to this appeal, BSC filed a motion for summary judgment of invalidity of the asserted claims of the 1997 patents and the '662 patent under 35 U.S.C. § 112. *Id.* at 551-52. BSC argued that the asserted claims of the patents-in-suit are invalid for nonenablement, lack of adequate written description and indefiniteness.[2] *Id.* at 552.

A. The 1997 Patents

The district court granted summary judgment that the 1997 patents are invalid for nonenablement, *id.* at 557, and for failure to meet the written description requirement, *id.* at 555. Addressing written description, the district court determined that the 1997 patents disclose that the claimed analogs must have structural similarity to rapamycin (*i.e.*, they must be macrocyclic lactones). *Id.* at 554. However, the district court also noted that "this disclosure in no way restricts the universe of potential analogs fitting the limitations as construed by the court." *Id.* In a claim construction order issued concurrently with its decision on the summary judgment motion, the district court construed the phrase

[2] Claims 1, 2, 5, 6, 40, 41, 44, 47, and 48 of the '3286 patent are not at issue in this appeal because the parties entered into a covenant not to sue. *Id.* at 543. All other claims of the patents-in-suit are at issue.

"rapamycin or a macrocyclic lactone analog thereof" as meaning "sirolimus or a macrocyclic lactone molecule with a structure similar to sirolimus." Markman at *2.

The district court also determined that the specification fails to disclose any formulae or structures of any specific analog or provide any "definitions, examples, or experimental models . . . for determining whether a compound is a structurally similar analog as contemplated by the patentees." *Boston Scientific Corp.*, 679 F. Supp. 2d at 554. The district court acknowledged that at the time of filing, a small number of macrocyclic lactone analogs of rapamycin were known. *Id.* However, the district court, without finding a specific quantity, noted that there is "a general agreement among the parties that there are numerous potential analogs of rapamycin." *Id.* at n.23.

The district court recognized that Appellants' experts opined that the specification discloses that the analogs must have a particular function – the inhibition of cell-cycle progression – and that a person of ordinary skill in the art could identify structurally similar analogs with the same function. *Id.* at 555. However, the district court determined that this testimony was insufficient because "describing certain functions of the genus of claimed analogs does not equate to a description of the claimed analogs themselves." *Id.*

The district court noted that the inventors testified they did not work with or test any analogs of rapamycin prior to filing, and "no evidence contradicts the inventors' deposition testimony or otherwise indicates that the inventors had possession of the full scope of the invention as claimed." *Id.* The court concluded that "[l]ogically, the inventors could not have described a knowledge that they did not possess." *Id.* The district court also concluded

that "no reasonable jury could find that the written description requirement has been met with respect to the claimed analogs." *Id.* The district court also held that the 1997 patents are invalid for nonenablement.

B. The '662 Patent

The district court next addressed the '662 patent. In its claim construction order, the district court had construed "macrocyclic triene analog" to mean "a macrocyclic triene molecule with a structure similar to rapamycin and that binds FKBP12." Markman at *2. The district court determined that the '662 patent gives more detail, as compared to the 1997 patents, regarding the mechanism of action of rapamycin. *Boston Scientific Corp.*, 679 F. Supp. 2d at 558 n.37. The district court found that, unlike the 1997 patents, "the '662 patent explains that rapamycin binds FKBP12 which, in turn, binds to and inhibits the kinase TOR; this mechanism of action serves to inhibit neointimal hyperplasia and reduce restenosis." *Id.* at 557-58.

However, the district court further noted that:

> Notwithstanding the above disclosure, no macrocyclic triene analogs are named, structurally depicted, exemplified, or otherwise described in the '662 patent specification. No assays or other experimental models are provided with respect to testing an analog candidate's ability to function as rapamycin, that is, to bind FKBP12 which, in turn, binds to and inhibits the kinase TOR. . . .
>
> Thus, although limited by function, the claims of the '662 patent are drawn to a genus of macrocyclic triene analogs without any description of any species within the genus. The Federal Circuit has required the identification of "sufficient species" to

> show that the totality of a claimed genus was invented and disclosed.

Id. at 558 (citing *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d. 1115, 1126 (Fed. Cir. 2008)). The district court determined that under our precedent "a 'definition by function' does not suffice to define or describe the genus" even if it allows one of skill to "guess and check" what analogs could potentially work. *Id.* at 558-59 (citing *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002)).

The district court acknowledged that "some macrocyclic triene analogs were known in the art" but found that this "does not alleviate [Appellants'] obligation under § 112 to provide an example." *Id.* at 559. The district court concluded that "[t]he inventors were required to describe at least one representative macrocyclic triene analog; having failed to do so, the '662 patent is [therefore] invalid for lack of written description." *Id.* Thus, the district court granted BSC's motion for summary judgment of invalidity of the '662 patent for lack of adequate written description. *Id.* The district court did not separately rule on whether the '662 patent is also invalid for lack of enablement. *Id.* at n.41. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).[3]

DISCUSSION

Appellants argue that the district court improperly granted BSC's motion for summary judgment of invalidity

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[3] Appellants asserted the patents-in-suit against Abbott Cardiovascular Systems, Inc., in four civil actions before the District of New Jersey. On January 27, 2010, the district court in New Jersey entered a judgment against Appellants after concluding that their arguments were collaterally estopped by the decision of the District of Delaware that is now before us.

of the '7286 patent, the '3286 patent, the '473 patent and the '662 patent under 35 U.S.C. § 112. Summary judgment is appropriate "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(c). We review a district court's grant of summary judgment *de novo*, reapplying the appropriate standard applicable before the district court. *See, e.g.*, *Univ. of Rochester v. G. D. Searle & Co.* 358 F.3d 916, 919-20 (Fed. Cir. 2002). Because issued patents are presumed valid, 35 U.S.C. § 282, a party seeking to invalidate a patent must submit clear and convincing evidence of invalidity. *Id.* at 920. In deciding a motion for summary judgment, "[t]he evidence of the nonmovant is to be believed, and all justifiable inferences are to be drawn in his favor." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986). "Compliance with the written description requirement is a question of fact but is amenable to summary judgment in cases where no reasonable fact finder could return a verdict for the non-moving party." *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1307 (Fed. Cir. 2008).

Section 112, paragraph 1, requires that the specification contain a written description of the invention. 35 U.S.C. § 112, ¶ 1. "[T]he hallmark of written description is disclosure." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). A specification adequately describes an invention when it "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* at 1351. "A 'mere wish or plan' for obtaining the claimed invention is not adequate written description." *Centocor Ortho Biotech, Inc. v. Abbott Labs*, 636 F.3d 1341, 1348 (Fed. Cir. 2011).

I. The 1997 Patents

The parties dispute whether the shared specification of the 1997 patents contains adequate written description regarding the claimed genus of macrocyclic lactone analogs of rapamycin. Appellants argue that the specification's description of macrocyclic lactone analogs was sufficient to satisfy the written description requirement in light of the state of the art as of the effective filing date. Appellants contend that they submitted detailed evidence regarding the state of the art that precludes a finding on summary judgment. For example, Appellants relied on the declaration of their expert witness Dr. David Sabatini as well as publications that they allege demonstrate: 1) that the structure and the mechanism of action of rapamycin were known; 2) that the correlation between the structural elements of rapamycin and its mechanism of action and biological activity was known; 3) that dozens of rapamycin analogs having the same macrocyclic ring structure as rapamycin and comparable biological activity were known; and 4) that persons of ordinary skill knew of assays to determine if analogs had the same mechanism of action as rapamycin and thus would also inhibit cell proliferation. Appellants' Br. 43-44.

Appellants contend that because information regarding the structure, mechanism of action, and biological activity of rapamycin and its analogs was set forth in the prior art, it was not necessary for the patent to disclose "formulae or structures" or set forth "definitions, examples, or experimental models" of particular macrocyclic lactone analogs. Instead, Appellants argue that the specification combined with the knowledge of one skilled in the art "provided a template for those of ordinary skill to use for identifying analogs falling within the scope of the claims." Appellants' Br. 45-46. Appellants, relying upon *In re Herschler*, 591 F.2d 693, 702 (CCPA 1979) and

In re Fuetterer, 319 F.2d 259 (CCPA 1963),[4] argue that when claiming a combination of known elements, as opposed to a novel compound, the specification "need not list examples" nor is any "comprehensive description" required. Appellants' Br. 32-34. Appellants argue that the claimed macrocyclic lactone analogs were sufficiently well known such that "the written description need be 'only so specific as to lead one having ordinary skill in the art to that class of compounds.'" *Id.* at 34 (quoting *Herschler*).

Appellants further contend that the prior art contained a known correlation between the structure of rapamycin and its analogs and their function. Appellants argue that because "functional claim language can meet the written description requirement when the art has established a correlation between structure and function," *Ariad*, 598 F.3d at 1350, the specification does not need to contain examples of specific macrocyclic lactone analogs of rapamycin.

BSC contends that the specification of the 1997 patents contains nothing to indicate that the inventors were in possession of the claimed inventions in 1997. BSC argues that, as construed by the district court, the "macrocyclic lactone analog" limitation represents a broad genus that covers any macrocyclic lactone molecule that is structurally similar to rapamycin. BSC contends that our precedent sets out a clear test to determine whether a specification adequately describes a claimed chemical genus:

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[4] *Fuetterer* is not binding precedent because only two judges on the five judge panel joined the opinion (Judge Martin concurred in the result only). 319 F.2d at 266.

> A written description of an invention involving a chemical genus, like a description of a chemical species, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials.

Regents of the Univ. of Cal. v. Eli Lilly & Co., 199 F.3d 1559, 1568 (Fed. Cir. 1997) (hereinafter, *Eli Lilly*).

BSC argues that the specification of the 1997 patents fails to meet this test. BSC notes that there are no examples of "macrocyclic lactone analogs" of rapamycin in the patents. BSC also argues that the patents fail to disclose the structures or features that render a molecule sufficiently similar to rapamycin to classify it as a "macrocyclic lactone analog." BSC contends that because the specification fails to disclose any of this essential information, there is nothing in the 1997 patents showing that the inventors possessed drug-eluting stents employing the broad genus of claimed macrocyclic lactone analogs. Additionally, BSC contends that upon consideration of "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology [and] the predictability of the aspect at issue," *Ariad*, 598 F.3d 1359, the specification's description of macrocyclic lactone analogs is insufficient.

We agree with BSC that no reasonable jury could conclude that there is sufficient written description support for the asserted claims of the 1997 patents. "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Eli Lilly*, 199 F.3d at 1568

(quoting *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993)).

We have "held that a sufficient description of a genus requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Ariad*, 598 F.3d at 1350. Because each individual invention "has a novel relationship with the state of the art from which it emerges" we have declined to "set out any bright-line rules governing, for example, the number of species that must be disclosed to describe a genus claim . . . ." *Id.* at 1351. The appropriate number of species that one must disclose when claiming a genus "necessarily changes with each invention, and it changes with progress in a field." *Id.*

What is required to meet the written description requirement "varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005). As our en banc court explained in *Ariad*, "[f]or generic claims, we have set forth a number of factors for evaluating the adequacy of the disclosure, including 'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.'" *Ariad*, 598 F.3d at 1351 (citing *Capon*, 418 F.3d at 1359).

Turning to the specification's disclosure of macrocyclic lactone analogs of rapamycin, we agree with BSC that no reasonable jury could conclude that the inventor possessed the claimed subject matter. The shared specification of the 1997 patents contains virtually no information regarding macrocyclic lactone analogs of rapamycin. The

sole mention of the analogs outside of the claims (that the applicant added nine years after the effective filing date) is under the heading "Experiments." '7286 patent col.6 ll.4-5. The shared specification lists "Agents: Rapamycin (sirolimus) structural analogs (macrocyclic lactones) and inhibitors of cell cycle progression." *Id.* Then four experimental delivery methods using only rapamycin are detailed. No experiments are detailed using macrocyclic lactone analogs nor does the specification even indicate performance of any such experiments. An *ipsis verbis* disclosure of a claimed genus (under the heading Experiments) is not *per se* sufficient to meet the written description requirement. *Enzo Biochem*, 323 F.3d at 968. While the shared specification demonstrates possession of rapamycin in the claimed stent, it does not evidence possession of the genus of macrocyclic lactone analogs of rapamycin in the claimed invention to inhibit restenosis.

Although examples are not always required to satisfy the written description requirement, the lack of any disclosure of examples may be considered when determining whether the claimed invention is adequately described. The 1997 patents contain no examples of macrocyclic lactone analogs of rapamycin, and give no guidance on how to properly determine whether a compound is a macrocyclic lactone analog of rapamycin besides vaguely indicating they must be "structural[ly] similar" to rapamycin. Given the structural complexity of rapamycin (rapamycin contains fifty-one carbon atoms, seventy-nine hydrogen atoms, thirteen oxygen atoms and a nitrogen atom), the universe of potential compounds that are structurally similar to rapamycin and classifiable as macrocyclic lactones is potentially limitless. As noted by the district court, the Appellants do not specifically contest that tens of thousands of potential macrocyclic lactone analogs exist. *Boston Scientific*, 679 F. Supp. 2d

at 554 n.23. Furthermore, even the minor structural changes to the molecular structure of rapamycin that are necessary to create analogs may have significant and unpredictable effects on functionality. J.A. 1764; J.A. 1769.

It is true that some species of this vast genus were known in the art. For example, both the Cottens publication and the Skotnicki patent disclosed specific species of the claimed genus of macrocyclic lactone analogs. Any suggestion that these references represented existing knowledge in the art so well known as to excuse including a more detailed disclosure of the macrocyclic lactone analogs genus in the specification is belied by the state of the art at the time of the invention. *Cf. Ariad*, 598 F.3d at 1354-55 (inventor has obligation to disclose molecules when the art is unpredictable and existing knowledge scant).

At the effective filing date, very little knowledge existed regarding the use of drug-eluting stents to inhibit restenosis. In fact, Cordis's Cypher® stent, which employs the patented technology, was the first drug-eluting stent marketed and approved in the United States. Appellants' own expert declarations detail the failure of others to develop drug-eluting stents to inhibit restenosis and evidenced the "highly unexpected" and "remarkable clinical results seen in Cordis's Cypher® stent." J.A. 14739-46; J.A. 14872-73. Appellants also argued in their briefing in opposition to BSC's § 103 summary judgment motion that the state of the art was highly unpredictable. J.A. 14698 ("[P]ersons of ordinary skill were faced with a multitude of possible therapeutic approaches and a multitude of possible drug and polymer combinations. Additionally, these proposed solutions were anything but predictable. Researchers in the field had little idea which, if any would prove successful.").

Indeed, the shared specification of the 1997 patents acknowledges the uncertainties surrounding rapamycin, restenosis, and drug-eluting stents as of the effective filing date of the patents. *See, e.g.*, '7286 patent col.1 ll.38-40 ("The exact hormonal and cellular processes promoting restenosis are still being determined."); *id.* col.2 ll.49-52 ("The exact mechanism for restenosis is still under active investigation."); *id.* col.1 ll.54-56 ("The mechanisms for most agents employed [to prevent smooth muscle cell proliferation] are still unclear."); *id.* col.5 ll.59-60 ("The ideal agent for restenosis has not yet been identified."); *id.* col.5 ll.36-38 ("The precise mechanism of rapamycin is still under active investigation.").

This case, in many respects, parallels our decision in *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d. 1115, 1126 (Fed. Cir. 2008). In *Carnegie Mellon*, the court held that our case law regarding generic claims is applicable to both inventions claiming novel genera of chemical and biological compounds as well as inventions claiming combinations of prior art compounds with other elements. 541 F.3d at 1124. In *Carnegie Mellon*, the patentee argued that our holding in "*Eli Lilly* is distinguishable from the present case because the invention in *Eli Lilly* was tied to a specific cDNA sequence, whereas the invention here involves a combination of well known elements that create a generic biotechnological tool." *Id.* at 1122-23. The patentee argued that species of the claimed genus "were well known in the art" and that the district court in granting summary judgment of no written description "failed to draw inferences in [the patentee's] favor." *Id.* at 1123. We rejected these arguments in *Carnegie Mellon* and likewise find them unavailing here. The test for written description is the same whether the claim is to a novel compound or a novel combination of known elements. The test is the same whether the claim

element is essential or auxiliary to the invention. *Cf. Aro Mfg. Co. v. Convertible Top Replacement Co.*, 365 U.S. 336, 345 (1961) ("[T]here is no legally recognizable or protected 'essential' element, 'gist' or 'heart' of the invention in a combination patent.").

We conclude that in this case, like *Carnegie Mellon*, summary judgment was appropriately granted. In *Carnegie Mellon*, the court noted that only three bacterial genes out of thousands of species had been cloned, and only one was disclosed in the specification. 541 F.3d at 1125. The court contrasted *Carnegie Mellon* with *Capon*, a case where the prior art contained "extensive knowledge of the nucleotide structure" of the relevant DNA including 785 mouse antibody DNA light chains and 1,327 mouse antibody DNA heavy chains. *Id.* Here, no analogs are disclosed in the specification. While a small number of such analogs were known in the prior art, the claims cover tens of thousands of possible macrocyclic lactone analogs. With no guidance at all in the specification as to how to properly identify or choose the claimed analogs, and in light of the unpredictability and nascent state of using drug-eluting stents to treat restenosis, we agree with the district court that appellants have failed to create genuine issues of material fact.

Although it is true that functional claim language can meet the written description requirement when there is an established correlation between structure and function, Appellants fail to establish any such correlation. *See, e.g.*, *Univ. of Rochester*, 358 F.3d at 925 (explaining that "functional descriptions of genetic material can, in some cases, meet the written description requirement if the functional characteristics are coupled with a known or disclosed correlation between function and structure") (citations and internal quotations omitted). Appellants contend that the declaration of Dr. Sabatini and prior art

patents and articles indicate that "the structure and mechanism of action of rapamycin were known" and that "the correlation between the structural elements of rapamycin and its mechanism of action and biological activity was known." *See, e.g.*, Appellants' Br. at 43-44. In particular, Appellants rely on a July 1996 article from *Science* (the Choi article) that discloses how rapamycin interacts with FKBP12 and mTOR. J.A. 11162-65. However, both the Choi article and Dr. Sabatini's declaration directly conflict with the shared specification of the 1997 patents, which explicitly states that "the precise mechanism of rapamycin *is still under active investigation*." '7286 patent col.5 ll.36-38 (emphasis added).

The shared specification indicates that the alleged correlation between structure and function was not well known by the effective filing date. Dr. Sabatini's declaration explains that, based on the Choi article, rapamycin must first bind to FKBP12 via rapamycin's pipecolinyl ring to form a rapamycin/FKBP12 complex in order to inhibit restenosis. J.A. 10556. Then this rapamycin/FKBP12 complex binds with mTOR. *Id.* Specifically, rapamycin's triene group interacts with mTOR. *Id.* Therefore, Dr. Sabatini's declaration indicates that rapamycin's *structural* features that allow it to *function* to inhibit restenosis are: 1) the pipecolinyl ring and 2) the triene group. However, the specification of the 1997 patents is silent about the need for the claimed analogs to maintain these two structural features.

When determining whether a specification contains adequate written description, one must make an "objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Ariad*, 598 F.3d at 1351. Because the specification is viewed from the perspective of one of skill, in some circumstances, a patentee may rely on information that is

"well-known in the art" for purposes of meeting the written description requirement. *See Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357 1366-68 (Fed. Cir. 2006). However, when the four corners of the specification directly contradict information that the patentee alleges is "well-known" to a person of skill at the effective filing date, no reasonable jury could conclude that the patentee possessed the invention. Here, the specification of the 1997 patents itself refutes any conclusion that "the structural elements of rapamycin and *its mechanism of action* and biological activity was known." *See Univ. of Rochester*, 358 F.3d at 930 ("Although section 282 places the burden of proof on the party seeking to invalidate a patent, it does not foreclose the possibility of that party demonstrating that the patent in suit proves its own invalidity."). Thus, there is insufficient correlation between the function and structure of rapamycin and its analogs to provide adequate written description support for the entire genus of macrocyclic lactone analogs of rapamycin.

Given the absence of information regarding structural characteristics of macrocyclic lactone analogs or examples of macrocyclic lactone analogs in the specification, the unpredictability of the art and the nascent state of using drug-eluting stents to inhibit restenosis, we affirm the district court's grant of summary judgment. The patent laws do not reward an inventor's invitation to other researchers to discover which of the thousands of macrocyclic lactone analogs of rapamycin could conceivably work in a drug-eluting stent. Because we affirm the district court's holding that no reasonable jury could conclude that the 1997 patents contained sufficient written description support, we need not separately address Appellants' arguments regarding enablement.

II. The '662 Patent

The '662 patent claims "rapamycin or a macrocyclic triene analog thereof" in combination with specific drug-eluting stents. Therefore, we must analyze whether a reasonable juror could conclude that the inventors of the '662 patent were in possession of the claimed genus of "macrocyclic triene analogs" in combination with the other claim elements. Although Appellants make many of the same arguments regarding the '662 patent as they did for the 1997 patents, Appellants argue that the '662 patent sets forth even more information regarding rapamycin and its analogs. We agree with the district court that no reasonable juror could determine that the specification adequately describes the claimed genus of "macrocyclic triene analogs."

As shown by Appellants' own experts, at the effective filing date of the '662 patent, researchers continued to struggle to find compounds that would work in a drug-eluting stent to prevent restenosis. J.A. 14739-46; J.A. 14872-73. Therefore, at the time of effective filing date of the '662 patent, such technology was still in its infancy. Despite this fact, the '662 patent fails to disclose even a single member of either the genus of "analogs" of rapamycin, or the more specific genus of "macrocyclic triene analogs" of rapamycin. In fact, even though the specification of the '662 patent contains more information regarding rapamycin and discloses the broad genus of "analogs" of rapamycin, it *never* discloses the sub-genus of "macrocyclic triene analogs" of rapamycin. Instead, the only mention of the term "macrocyclic triene" in the patent specification is the statement that "[r]apamycin is a macroyclic [sic] triene antibiotic." '662 patent col.5 l.31.

In *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996), we addressed the written description require-

ment in a situation where a patentee claimed a sub-genus that was not disclosed *ipsis verbis* in the specification. There, as here, instead of disclosing the sub-genus, the patentee disclosed only the broader genus. *Id.* We held that in the absence of blaze marks "as to what compounds other than those disclosed as preferred, might be of special interest . . . simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to particular species or sub-genuses." *Id.* at 1570-71. Here, the inventors similarly disclosed a genus (analogs of rapamycin), but claimed a narrower sub-genus (macrocyclic triene analogs of rapamycin). However, nothing in the '662 patent indicates that the claimed triene analogs might be of special interest. Given the nascent state of using drug-eluting stents to treat restenosis at this time, the lack of such blaze marks in the '662 patent prevents any conclusion that the patent contains sufficient written description of the claimed triene analogs of rapamycin. No reasonable juror could determine that the specification "reasonably convey[s] to persons skilled in the art that the inventor had possession" of the claimed sub-genus. *Id.* at 1570.

Moreover, the functional disclosures in the '662 patent fail to sufficiently describe the claimed sub-genus of macrocyclic triene analogs or provide sufficient blaze marks as to which analogs might successfully work in drug-eluting stents. Even at the 2001 effective filing date, the relationship between the function of rapamycin and its structure was not so well known that it excuses the patentee's failure to explicitly disclose the claimed sub-genus or any species within the sub-genus. Like the 1997 patents, the '662 patent confirms that the mechanism of action of rapamycin was not well known at the effective filing date. Although the patent explains the binding of rapamycin to FKBP12 to form a complex and the subse-

quent binding of this complex to mTOR, the patent also admits that "[t]he molecular events that are responsible for the actions of rapamycin, a known anti-proliferative, which acts to reduce the magnitude and duration of neointimal hyperplasia, are still being elucidated." '662 patent col.5 l.62 – col.6 l.3.

Furthermore, the '662 patent states that "[r]apamycin functions to inhibit smooth muscle cell proliferation through a number of mechanisms." *Id.* col.5 ll.43-44. The patent then gives details regarding how the compound and its analogs function, including stating that "there is evidence that rapamycin may also inhibit the other major component of restenosis, namely, negative remodeling." *Id.* col.6 ll.12-14. However, the specification states that it is unknown how rapamycin functions to inhibit negative remodeling:

> It may be hypothesized that rapamycin acts to reduce negative remodeling in several ways. By specifically blocking the proliferation of fibroblasts in the vascular wall in response to injury, rapamycin may reduce the formation of vascular scar tissue. Rapamycin may also affect the translation of key proteins involved in collagen formation or metabolism.

Id. col.7 ll.22-27. Thus, the '662 patent indicates that the mechanism of action corresponding to the function of rapamycin and its analogs is still under investigation. As with the 1997 patents, this characterization of the state of the art directly contradicts Appellants' assertion that there was a well known correlation between the structure of rapamycin and its function.

The '662 patent also contains insufficient support for the highly specific functional requirements claimed. For example, claim 1, which is representative of all of the

independent claims of the '662 patent, requires "from about 64 μg to about 197 μg of rapamycin or a macrocyclic triene analog thereof . . . wherein said device provides an in-stent late loss in diameter at 12 months following implantation in a human of less than about 0.5 mm[.]" The '662 patent includes no information suggesting how a person of skill in the art would select macrocyclic triene analogs with such highly specific performance requirements. There is also no indication of which structural features of analogs of rapamycin are necessary to achieve these results. Although it is possible that one could use trial and error, one would have to wait a full year in order to determine whether a specific analog in combination with the other claimed elements achieved the claimed results. The specification fails to convey to one of skill in the art that the inventors were in possession of any analogs that achieve these highly specific results as the written description requirement mandates.

Given the state of the art, and the lack of any successful combination of elements, a person of skill in the art would expect more than the meager disclosure of "analogs" in the '662 patent. The specification fails to disclose the sub-genus of "macrocyclic triene analogs" by name, by functionality, or even by implication. The specification similarly fails to disclose a single species of "macrocyclic triene analogs" or a single species of any analog of rapamycin. Furthermore, the plethora of test results in the '662 patent are devoted exclusively to rapamycin itself, with no results from the testing of analogs. Given the paucity of disclosure regarding the claimed sub-genus, no reasonable juror could conclude that the specification of the '662 patent discloses to a person of ordinary skill in the art that the inventors were in possession of the claimed invention.

CONCLUSION

We hold that no reasonable juror could determine that the asserted claims of the patents-in-suit contain adequate written description of the claimed analogs of rapamycin. Therefore, we affirm the judgment of the district court.

AFFIRMED

United States Court of Appeals for the Federal Circuit

BOSTON SCIENTIFIC CORPORATION AND BOSTON SCIENTIFIC SCIMED, INC.,
Plaintiffs-Appellees,

v.

JOHNSON & JOHNSON (ALSO KNOWN AS JOHNSON & JOHNSON, INC.), CORDIS CORPORATION, AND WYETH,
Defendants-Appellants,

2010-1230, -1231, -1233, -1234

Appeals from the United States District Court for the District of Delaware in consolidated case nos. 07-CV-0333, 07-CV-0348, 07-CV-0409, and 07-CV-0765, Judge Sue L. Robinson

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GAJARSA, *Circuit Judge*, concurring-in-part.

I agree with the majority that the asserted claims of U.S. Patent Nos. 7,217,286 (the "'7286 patent"); 7,223,286; 7,229,473 (collectively, the "1997 patents"); and 7,300,662 (the "'662 patent") are invalid, but would hold the 1997 patents invalid for lack of enablement. Therefore, I concur only in judgment as to the 1997 patents. I join fully the majority's opinion regarding the '662 patent.

The claimed invention is a combination of a stent, polymeric carrier, and therapeutic agent. The majority focuses solely on the written description aspect of whether the therapeutic agent's analogs were adequately described and ignores that in nearly all of the asserted claims, the agents must effectively inhibit neointimal proliferation. Because undue experimentation was required to practice the 1997 patents, the district court's grant of summary judgment of invalidity should have been affirmed on enablement grounds.

The enablement requirement of 35 U.S.C. § 112 ¶ 1 is the appropriate tool for invalidating claims that are broader than their disclosure. The majority blurs the line between enablement and written description and does not address the claim language that "rapamycin, or a macrocyclic lactone analog thereof, and is present in an amount *effective to inhibit neointimal proliferation*." '7286 patent, col.8 ll.15-23 (emphasis added).

The majority's opinion further extends the written description requirement into the realm of enablement. Much of the confusion in this case is due to the difficulty of determining what constitutes a genus or a subgenus, the relationship between the structure and the function of compounds, and how the written description requirement applies to novel compounds as opposed to novel combinations of known elements. These are legal inquiries predicated on disputed issues of material fact. Applying the enablement requirement would help to clear the thicket of jurisprudence regarding § 112 ¶ 1. As discussed briefly below, in this case, the enablement analysis is simpler and more appropriate.

The relevant test for enablement is whether the specification enables one of skill in the art to practice the claimed invention without undue experimentation. *In re*

Wands lists the factors to be considered in determining whether a disclosure would require undue experimentation. 858 F.2d 731, 737 (Fed. Cir. 1988). The district court correctly applied the *Wands* factors and held that practicing the claimed invention with a macrocyclic lactone analog would have required undue experimentation in 1997. The district court noted that "there is no direction or guidance disclosed in the patents and no working examples" (factors 2 and 3); "the claims are moderately broad insofar as there is no limit, aside from function (determined through experimentation), regarding the number of potential analogs" (factor 8); "there is no genuine dispute that the invention concerns a very complex chemical and biomechanical art germane to highly skilled cardiologists" (factors 4 and 6); "the 1997 patents were filed on the heels of a decade marked by failed attempts to reduce restenosis" (factor 5); and "the chemical arts have long been acknowledged to be unpredictable" (factor 7). *Boston Scientific v. Johnson & Johnson*, 679 F. Supp. 2d 539, 557 (D. Del. 2010). These findings were consistent with Appellants' opposition to Appellees' § 103 motion. The Appellants argued that "the development of the Cypher stent required trial-and-error experimentation with many drugs and polymers." J.A. 17718.

To satisfy a majority of the asserted claims, a rapamycin analog not only needs to generally prevent restenosis, but must also prevent restenosis when used on a drug-eluting stent. Once rapamycin's structure was known, scientists could hypothesize that useful analogs could potentially be created by changing parts of that molecule, particularly outside of the critical macrocyclic ring structure. The 1997 patents did not need to explain how to synthesize, identify, or determine the biological

activity of a suitable macrocyclic lactone analog. The patents did, however, need to disclose where the rapamycin molecule should be modified to obtain a suitable analog with the desired efficacy *in stents*. It is not enough that a person of ordinary skill in 1997 could have readily determined whether a compound was a claimed macrocyclic lactone; for most of the claims, the analog needed to prevent restenosis when used on a drug eluting stent. Because no one knew of any rapamycin analogs with the desired efficacy when delivered by stents as of the filing date of the 1997 patents, Appellants' claims are not enabled.

The claims of the 1997 patents are invalid for lack of enablement but because the majority decided that the asserted claims were invalid solely for lack of written description, I concur only in the judgment as to those patents.