601 F.3d 1359, 95 U.S.P.Q.2d 1031
(Cite as: 601 F.3d 1359)

United States Court of Appeals,
Federal Circuit.
NOVO NORDISK A/S and Novo Nordisk, Inc.,
Plaintiffs-Appellants,
v.
CARACO PHARMACEUTICAL LABORATORIES, LTD., and Sun Pharmaceutical Industries, Ltd., Defendants-Appellees.

No. 2010-1001.
April 14, 2010.

Background: Patentee brought action against generic drug manufacturer, alleging infringement of patent for blood glucose-lowering drug. The United States District Court for the Eastern District of Michigan, Avern Cohn, J., 656 F.Supp.2d 729, entered an injunction directing patentee to request the Food and Drug Administration (FDA) to replace patentee's patent use code listing for the drug in the Orange Book with the former listing, and patentee appealed.

Holding: The Court of Appeals, Rader, Circuit Judge, held that Hatch-Waxman Act provided a limited counterclaim to a generic manufacturer in an infringement action only if the drug patent did not claim any approved methods of using the listed drug, and therefore counterclaim was not available on ground that drug patent did not claim "all approved methods."

Reversed and vacated.

Clevenger, Circuit Judge, filed concurring opinion.

Dyk, Circuit Judge, filed dissenting opinion.

West Headnotes

[1] Federal Courts 170B 814.1

170B Federal Courts
170BVIII Courts of Appeals
170BVIII(K) Scope, Standards, and Extent
170BVIII(K)4 Discretion of Lower Court
170Bk814 Injunction
170Bk814.1 k. In general. Most Cited Cases

Court reviews the grant of an injunction for an abuse of discretion.

[2] Federal Courts 170B 754.1

170B Federal Courts
170BVIII Courts of Appeals
170BVIII(K) Scope, Standards, and Extent
170BVIII(K)1 In General
170Bk754 Review Dependent on Whether Questions Are of Law or of Fact
170Bk754.1 k. In general. Most Cited Cases

To the extent that an injunction is premised upon an issue of law, such as statutory interpretation, court reviews that issue without deference.

[3] Statutes 361 188

361 Statutes
361VI Construction and Operation
361VI(A) General Rules of Construction
361k187 Meaning of Language
361k188 k. In general. Most Cited Cases

Statutes 361 217.4

361 Statutes
361VI Construction and Operation
361VI(A) General Rules of Construction
361k213 Extrinsic Aids to Construction
361k217.4 k. Legislative history in general. Most Cited Cases

To overcome the plain meaning of a statute, the party challenging it must establish that the legislative history provides an extraordinary showing of contrary intentions.

[4] Health 198H 319

198H Health
198HI Regulation in General
198HI(E) Drugs; Medical Devices and Instruments
198Hk315 Applications and Approvals
198Hk319 k. Generic and orphan drugs; market exclusivity. Most Cited Cases

Hatch-Waxman Act provided a limited counterclaim to a generic manufacturer in an infringement action only if the drug patent did not claim any approved methods of using the listed drug; counterclaim was not available on ground that drug patent did not claim "all approved methods." Federal Food, Drug, and Cosmetic Act, § 505(j)(5)(C)(ii)(I), 21 U.S.C.A. § 355(j)(5)(C)(ii)(I).

[5] Health 198H 319

198H Health
198HI Regulation in General
198HI(E) Drugs; Medical Devices and Instruments
198Hk315 Applications and Approvals
198Hk319 k. Generic and orphan drugs; market exclusivity. Most Cited Cases

Counterclaim provision of Hatch-Waxman Act only authorizes suits to correct or delete an erroneous drug patent number or expiration date, and authorization does not extend to the use code narrative. Federal Food, Drug, and Cosmetic Act, § 505(j)(5)(C)(ii)(I), 21 U.S.C.A. § 355(j)(5)(C)(ii)(I).

[6] Patents 291 283(1)

291 Patents
291XII Infringement
291XII(B) Actions
291k283 Defenses
291k283(1) k. In general. Most Cited Cases

Patent misuse doctrine may apply where the patentee's misconduct toward unrelated parties amounted to unfair market benefits beyond the scope of the patent.

Patents 291 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original utility. Most Cited Cases

Patents 291 328(4)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(4) k. Reissue. Most Cited Cases

6,677,358. Cited.

37,035. Cited.

***1360** Mark A. Perry, Gibson, Dunn & Crutcher LLP, of Washington, DC, argued for plaintiffs-appellants. With him on the brief were Josh A. Krevitt, of New York, NY; Wayne Barsky, of Los Angeles, CA; and Michael A. Sitzman, of San Francisco, CA.

James F. Hurst, Winston & Strawn LLP, of Chicago, IL, argued for defendants-appellees. With him on the brief were Charles B. Klein and Scott H. Blackman, of Washington, DC; David S. Bloch, of San Francisco, CA. Of counsel was Andrew Nichols, of Washington, DC.

Before RADER, CLEVENGER, and DYK, Circuit Judges.

Opinion for the court filed by Circuit Judge RADER. Concurring opinion filed by Circuit Judge CLEVENGER. Dissenting opinion filed by Circuit Judge DYK.

The United States District Court for the Eastern District of Michigan entered an injunction directing Novo Nordisk A/S and Novo Nordisk, Inc. (collectively, "Novo") to request the U.S. Food and Drug Administration ("FDA") to replace Novo's patent use code U-968 listing for Prandin ® in the Orange Book with the former U-546 listing. Because Caraco

Pharmaceutical Laboratories, Ltd. ("Caraco") does not have a statutory basis to assert a counterclaim requesting such injunctive relief, this court reverses and vacates the injunction.

I.

This case arises under the Drug Price Competition and Patent Term Restoration Act of 1984, Pub.L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. §§ 355, 360cc; 35 U.S.C. §§ 156, 271), as amended by the Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub.L. No. 108-173, 117 Stat.2066 (2003) (collectively, the "Hatch-Waxman Act"). The Hatch-Waxman Act strikes a balance between two potentially competing policy interests-inducing pioneering development of pharmaceutical formulations and methods and facilitating efficient transition to a market with low-cost, generic copies of those pioneering inventions at the close of a patent term. *See Andrx Pharms., Inc. v. Biovail Corp.,* 276 F.3d 1368, 1371 (Fed.Cir.2002).

Title 21 prohibits sale of a new drug without FDA approval. 21 U.S.C. § 355(a). To obtain that approval, a pioneering manufacturer must file a new drug application ("NDA"), containing clinical studies of the drug's safety and efficacy. 21 U.S.C. § 355(b)(1). As part of the NDA process, the manufacturer must also identify all patents that claim the drug or a method of use:

> The applicant shall file with the application *the patent number* and the *expiration date* of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in ***1361** the manufacture, use, or sale of the drug.
>
> 21 U.S.C. § 355(b)(1)(G) (emphases added).

> If *the patent information described in subsection (b)* of this section could not be filed with the submission of an application under subsection (b) of this section ..., the holder of an approved application shall file with the Secretary *the patent number* and *the expiration date* of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.
>
> 21 U.S.C. § 355(c)(2) (emphases added).

The FDA has authority to promulgate regulations for the efficient enforcement of these provisions. 21 U.S.C. § 371. Under those regulations, a pioneering manufacturer files with the FDA the patent number and the expiration date of any applicable patents by submitting Form 3542a ("Patent Information Submitted with the Filing of an NDA, Amendment, or Supplement") or Form 3542 ("Patent Information Submitted Upon and After Approval of an NDA or Supplement"). 21 C.F.R. § 314.53 (2009). If the patent claims one or more methods of using the NDA drug, Forms 3542a and 3542 require a description of each of those processes. *Id.* This description is commonly known as the "use code narrative." The FDA assigns a unique number, known as a "use code," to each description. The FDA publishes a list of drugs, along with the applicable patents and their associated use codes, in its Approved Drug Products With Therapeutic Equivalence Evaluations, commonly known as the "Orange Book."

A manufacturer that seeks to market a generic copy of these listed drugs may submit an abbreviated new drug application ("ANDA"). 21 U.S.C. § 355(j). The ANDA process streamlines FDA approval by allowing the generic manufacturer to rely on the safety and efficacy studies of a drug already listed in the Orange Book upon a showing of bioequivalence. 21 U.S.C. § 355(j)(2)(A)(iv).

As part of the ANDA process, a generic manufacturer must make a certification addressing each patent identified in the Orange Book pertaining to its drug. 21 U.S.C. § 355(j)(2)(A)(vii). Specifically, the generic manufacturer must select one of four alternatives permitting use of the patented product or process: (I) no such patent information has been submitted to the FDA; (II) the patent has expired; (III) the patent is set to expire on a certain date; or (IV) the patent is invalid or will not be infringed by the manufacture, use, or sale of

the generic drug. 21 U.S.C. § 355(j)(2)(A)(vii).

Often pharmaceutical formulations have multiple uses and applications. After expiration of the patent on the composition itself, only some of those uses may enjoy continued protection as patented methods. If a generic manufacturer wishes to seek FDA approval for a use not covered by a method-of-use patent for a listed drug, it must make a "section viii statement." 21 U.S.C. § 355(j)(2)(A)(viii). Along with the section viii statement, the generic manufacturer must submit a proposed label to the FDA that does not contain the patented method of using the listed drug. When considering approval of these requests for a use not covered by a patent, the FDA relies on the applicable patent's use code narrative to determine the scope of the patented method. *Applications for FDA Approval to Market a New Drug,* 68 Fed.Reg. 36676, 36682 (June 18, 2003). The FDA approves the section viii statement only where there is no overlap between the ***1362** proposed carve-out label submitted by the generic manufacturer and the use code narrative submitted by the pioneering manufacturer. *Id.*

The Hatch-Waxman Act facilitates early resolution of disputes between pioneering and generic manufacturers. To achieve this objective, the Act makes a Paragraph IV certification into an act of patent infringement. 35 U.S.C § 271(e)(2). A generic manufacturer that files a Paragraph IV certification must give notice to the patentee and the NDA holder and provide a detailed basis for its belief that the patent is invalid or not infringed. 21 U.S.C. § 355(j)(2)(B)(i). The patentee then has forty-five days to sue the generic manufacturer for infringement. 21 U.S.C. § 355(j)(5)(B)(iii). If the patentee does not sue, the FDA may approve the ANDA. If the patentee sues, the FDA may not approve the ANDA until expiration of the patent, resolution of the suit, or thirty months after the patentee's receipt of notice, whichever is earlier. 21 U.S.C. § 355(j)(5)(B)(iii). The court entertaining this suit has discretion to order a shorter or longer stay if "either party to the action fail[s] to reasonably cooperate in expediting the action." *Id.*

The Hatch-Waxman Act enables a generic manufacturer in a Paragraph IV suit to assert a counterclaim challenging the accuracy of the "patent information" submitted to the FDA:

> [The ANDA] applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) of this section on the ground that the patent does not claim either-
>
> (aa) the drug for which the application was approved; or
>
> (bb) an approved method of using the drug.

21 U.S.C. § 355(j)(5)(C)(ii)(I). This counterclaim provision was not part of the original Hatch-Waxman Act. Rather the Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub.L. No. 108-173, 117 Stat.2066 (2003) added this counterclaim provision to permit challenges to patent information at the FDA. The interpretation of this counterclaim provision is the central issue in this case.

II.

Novo markets and distributes the drug repaglinide under the brand name PRANDIN. PRANDIN is an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes (non-insulin dependent diabetes mellitus). The FDA has approved PRANDIN for three uses: (1) repaglinide by itself (i.e., monotherapy); (2) repaglinide in combination with metformin; and (3) repaglinide in combination with thiazolidinediones ("TZDs"). Novo Nordisk, Inc. holds the approved NDA for PRANDIN.

The Orange Book lists two patents for PRANDIN. U.S. Patent No. RE 37,035 (the "'035 patent") claims, *inter alia,* the chemical composition of repaglinide. The '035 patent expired on March 14, 2009. U.S. Patent No. 6,677,358 (the "'358 patent") claims, *inter alia,* repaglinide in combination with metformin:

> A method for treating non-insulin dependent diabetes mellitus (NIDDM) comprising administering to a patient in need of such treatment repaglinide in combination with metformin.

'358 patent, claim 4. The '358 patent expires on

June 12, 2018. Novo Nordisk A/S owns the '358 patent. Novo does not own patents claiming the other two approved methods of using repaglinide to treat type 2 diabetes. The FDA initially assigned the '358 patent the use code "U-546-Use ***1363** of repaglinide in combination with metformin to lower blood glucose."

On February 9, 2005, Caraco filed an ANDA for the drug repaglinide. The ANDA initially contained a Paragraph III certification for the '035 patent and a Paragraph IV certification for the '358 patent. On June 9, 2005, Novo initiated an infringement action against Caraco. In April 2008, Caraco stipulated that its ANDA would infringe the '358 patent if it included a label that discussed the combination of repaglinide and metformin. At around the same time, Caraco submitted an amended ANDA with a Paragraph IV certification for the '358 patent and a section viii statement declaring that Caraco was not seeking approval for the repaglinide-metformin combination therapy. The FDA indicated that it would approve Caraco's proposed carve-out label. Novo moved for reconsideration on the ground that allowing the carve-out would render the drug less safe and effective.

On May 6, 2009, Novo submitted an amended Form 3542 for PRANDIN in which Novo updated its use code narrative for the '358 patent. The FDA removed the use code U-546 from the Orange Book for PRANDIN and substituted the new use code "U-968-A method for improving glycemic control in adults with type 2 diabetes mellitus." The FDA then denied Novo's request for reconsideration as moot in light of the new use code. According to the FDA, the factual predicate on which the FDA's permissive carve-out determination had rested no longer applied. The FDA then disallowed Caraco's section viii statement, because its proposed carve-out label overlapped with the use code U-968 for the '358 patent. As a result, Caraco's current label now includes the repaglinide-metformin combination therapy, which is stipulated to infringe claim 4 of the '358 patent.

On June 11, 2009, Caraco amended its answer and counterclaim. Caraco added a counterclaim under 21 U.S.C. § 355(j)(5)(C)(ii), requesting an order requiring Novo to change the use code for the '358 patent in reference to PRANDIN from U-968 to U-546. Caraco claimed that the use code U-968 was overbroad because it incorrectly suggested that the '358 patent covered all three approved methods of using repaglinide even though it claimed only one approved method. Caraco also added a patent misuse defense, asserting that Novo misrepresented the scope of the '358 patent in its use code narrative.

On June 29, 2009, Novo moved to dismiss Caraco's new counterclaim and to strike the patent misuse defense. The district court denied Novo's motions. Caraco then moved for summary judgment on both the new counterclaim and the patent misuse defense. On summary judgment, the district court granted Caraco's motion on the counterclaim and declined to address the patent misuse defense. The district court found that Novo had improperly filed an overbroad use code narrative for the '358 patent. On September 25, 2009, the district court entered the following injunction:

> Novo Nordisk is hereby directed by mandatory injunction under 21 U.S.C. § 355(j)(5)(C)(ii)(1)(bb) to correct within twenty (20) days from the date of this Order and Injunction its inaccurate description of the '358 patent by submitting to FDA an amended Form FDA 3542 that reinstates its former U-546 listing for Prandin and describes claim 4 of the '358 patent in section 4.2b as covering the "use of repaglinide in combination with metformin to lower blood glucose."

Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd., 656 F.Supp.2d 729, 730 (E.D.Mich. 2009).

***1364** Given the urgency of Novo's situation, Novo filed a motion in this court for an expedited appeal from the district court's order. This court granted Novo's motion to expedite briefing. Novo also filed a motion for a stay of the injunction pending appeal and a stay of trial court proceedings. This court ordered a stay of the injunction pending disposition of this appeal but declined to stay trial court proceedings. Because the district court had jurisdiction under 28 U.S.C. §§ 1331 and 1338(e), this court has jurisdiction under 28 U.S.C. § 1292(c)(1).

III.

[1][2] This court reviews the grant of an injunction for an abuse of discretion. *Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.,* 424 F.3d 1293, 1301-02 (Fed.Cir.2005). To the extent that an injunction is premised upon an issue of law, such as statutory interpretation, this court reviews that issue without deference. *See Sanofi-Synthelabo v. Apotex, Inc.,* 470 F.3d 1368, 1374 (Fed.Cir.2006).

[3] Statutory construction "begins with 'the language of the statute.' " *Hughes Aircraft Co. v. Jacobson,* 525 U.S. 432, 438, 119 S.Ct. 755, 142 L.Ed.2d 881 (1999) (quoting *Estate of Cowart v. Nicklos Drilling Co.,* 505 U.S. 469, 475, 112 S.Ct. 2589, 120 L.Ed.2d 379 (1992)). This court derives the plain meaning of the statute from its text and structure. *Electrolux Holdings, Inc. v. United States,* 491 F.3d 1327, 1330 (Fed.Cir.2007) (citation omitted). If the statutory language is unambiguous, the inquiry ends. *Id.* Nevertheless, this court may "look at the legislative history 'only to determine whether a clear intent contrary to the plain meaning exists.' " *Sharp v. United States,* 580 F.3d 1234, 1238 (Fed.Cir.2009) (quoting *Glaxo Operations UK Ltd. v. Quigg,* 894 F.2d 392, 396 (Fed.Cir.1990)). To overcome the plain meaning of the statute, the party challenging it must establish that the legislative history provides "an 'extraordinary showing of contrary intentions.' " *Id.* (quoting *Garcia v. United States,* 469 U.S. 70, 75, 105 S.Ct. 479, 83 L.Ed.2d 472 (1984)).

IV.

[4] The Hatch-Waxman Act provides a limited counterclaim to a generic manufacturer in a Paragraph IV infringement action. The Act authorizes the generic manufacturer to assert a counterclaim "on the ground that *the patent does not claim* either (aa) the drug for which the application was approved; or (bb) *an approved method of using the drug.* " 21 U.S.C. § 355(j)(5)(C)(ii)(I) (emphases added).

Novo and Caraco agree that the '358 patent claims only one of the three approved methods of using PRANDIN (i.e., repaglinide in combination with metformin). Novo asserts that the counterclaim is available only if the ' 358 patent does not claim any approved methods. Caraco argues that it is entitled to the counterclaim because the '358 patent does not claim two of the approved methods of PRANDIN use. In other words, Novo reads "an approved method" in the counterclaim statute as "any approved method" while Caraco reads it as "all approved methods."

This court detects no ambiguity in the statutory language. When an indefinite article is preceded and qualified by a negative, standard grammar generally provides that "a" means "any." *See, e.g.,* American Heritage Dictionary of the English Language 1 (4th ed.2006) (defining "a" as "[a]ny" in the example "not a drop to drink"); Random House Webster's Unabridged Dictionary 1 (2d ed.2001) (defining the indefinite article "a" as "any" or "a single" in the example "not a one"); see also *Barnhart v. Thomas,* 540 U.S. 20, 26, 124 S.Ct. 376, 157 L.Ed.2d 333 (2003) (adopting a construction that is "quite sensible***1365** as a matter of grammar") (citation omitted).

The rest of the counterclaim provision also does not support Caraco's interpretation. In the context of this case, the statutory language "an approved method of using the drug" refers to the approved methods of using the listed drug, PRANDIN. This language cannot refer to the methods of using Caraco's generic drug, because the FDA has not yet approved Caraco's ANDA. Therefore, the Hatch-Waxman Act authorizes a counterclaim only if the listed patent does not claim any approved methods of using the listed drug.

Although the statutory language on its face presents no ambiguities, this court nonetheless examines the legislative history to make sure that it does not contain any clear intent to the contrary. Before the amendment to the Hatch-Waxman Act in 2003, private litigants could not challenge FDA submissions at all. *Buckman Co. v. Plaintiffs' Legal Comm.,* 531 U.S. 341, 349, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001). Novo and Caraco agree that the counterclaim provision responded to this court's decision in *Mylan Pharms., Inc. v. Thompson,* 268 F.3d 1323 (Fed.Cir.2002). In *Mylan,* the Orange Book listed a patent as covering the FDA-approved drug BuSpar. *Id.* at 1330-31. Mylan, a generic manufacturer, asserted that the patent "did not claim BuSpar or an approved method of using BuSpar." *Id.* at 1331. This

court held that Mylan did not have a private cause of action to delist the allegedly irrelevant patent from the Orange Book. *Id.* The 2003 amendment used exact language from Mylan in the new counterclaim provision. This choice of legislative language suggests that the 2003 Amendment sought to correct the specific issue raised in *Mylan,* i.e., to deter pioneering manufacturers from listing patents that were not related at all to the patented product or method. Thus, the language selected for this Amendment supports this court's interpretation that "an approved method" means "any approved method." A patent listing that covers one amongst several approved methods of using a formulation protects that patented method and thus bears a direct relation to the purpose of Orange Book listings. This court does not detect a situation such as the one occurred in *Mylan.*

This case also suggests that this court should address the relationship between section viii and the counterclaim provision. Section viii addresses scenarios where a patent claims at least one, but not all, approved methods of using a drug. *See* 21 U.S.C. § 355(j)(2)(A)(viii). This court recognizes that a broad use code covering all uses of a pharmaceutical could require generic manufacturers to prove specifically that their use will not overlap with and infringe the patented use. This proof, under Hatch-Waxman procedures, will take the form of a Paragraph IV lawsuit. In that context, the generic may provide proof that their use will not cause infringement of the patented use. This court perceives that the Hatch-Waxman Act will thus ensure that a generic drug for non-patented purposes will not be used for patented purposes via a simple section viii certification. Instead, the generic manufacturer will need to alleviate the risk of infringement or induced infringement in a proceeding that fully tests for infringement and its implications, including potential health and safety risks. Thus, the Act again facilitates efficient resolution of disputes concerning potential overlapping of protected and unprotected uses. The Act seeks to strike a balance of the pioneering and generic manufacturers' interests.

As Judge Clevenger points out, Caraco's real complaint should lie with the FDA, not with Novo. Had it not been for the FDA's regulatory action, Caraco could have asserted in a Paragraph IV lawsuit ***1366** that its proposed labeling did not infringe the '358 patent. It was the FDA, not Novo, that tipped the careful balance in the favor of pioneering manufacturers.

V.

[5] As further indication of balancing interests and creation of an efficient dispute resolution mechanism, this court notes that the Act, by its terms, does not allow generic manufacturers to counterclaim unless the listed patent bears no relation to the listed drug. To be more specific, the terms of the counterclaim provision do not authorize an order compelling the patent holder to change its use code narrative. The counterclaim provision states that a generic manufacturer can request an order compelling "the holder to correct or delete *the patent information* submitted by the holder under subsection (b) or (c)." 21 U.S.C. § 355(j)(5)(C)(ii)(I) (emphasis added). Subsection (b) requires a pioneering manufacturer to submit "*the patent number* and *the expiration* date of any patent ... which claims a method of using such drug." 21 U.S.C. § 355(b)(1) (emphases added). Subsection (c) states that "[i]f *the patent information* described in subsection (b) of this section could not be filed with the submission of an application," the holder "shall file with the Secretary *the patent number* and the *expiration date* of any patent ... which claims a method of using such drug." 21 U.S.C. § 355(c)(2) (emphases added).

Thus, the Act defined the term "patent information" as "the patent number and the expiration date." *See Valley Drug Co. v. Geneva Pharms. Inc.,* 344 F.3d 1294, 1296-97 (11th Cir.2003) (referring to the patent number and the expiration date as "this patent information"). The reference in subsection (c) to "the patent information described in subsection (b)" could only mean the patent number and the expiration date, because no other "patent information" appears in the statute. Therefore, to maintain consistency in the statutory terms, "the patent information" in the counterclaim provision must also mean the patent number and the expiration date. *Envtl. Def. v. Duke Energy Corp.,* 549 U.S. 561, 574, 127 S.Ct. 1423, 167 L.Ed.2d 295 (2007) (noting that the

identical words used in the same act are presumed to have the same meaning). Thus, the counterclaim provision only authorizes suits to correct or delete an erroneous patent number or expiration date. The authorization does not extend to the use code narrative. Once again, this careful use of language suggests that the Act facilitates efficient resolution of disputes over the potential overlap of patented and unpatented uses in the form of a Paragraph IV suit.

Approximately six months before the 2003 Amendment, the FDA promulgated a regulation concerning the "Submission of Patent Information" in which it requires a pioneering manufacturer to submit not only the patent number and the expiration date, but also the use code narratives and other patent-related information on Forms 3542a and 3542. *See* 21 C.F.R. § 314.53. This regulation appeared to include the use code narrative under the broader heading of "patent information." Although this regulation preceded the 2003 Amendment, it did not change the meaning of the statutory use of the term "patent information." As this court has clarified, "[s]uch opaque timing observations hardly amount to a 'most extraordinary showing of contrary intentions,' especially when the language of the statute trumpets its meaning by itself." *Wyeth v. Kappos,* 591 F.3d 1364, 1372 (Fed.Cir.2010). The counterclaim provision does not mention the FDA regulations or in any way suggest adoption of a meaning for "patent information" broader than the express statutory definition. Moreover, this court owes "no deference is due to agency interpretations at odds with the plain language of the statute ***1367** itself." *Pub. Employees Ret. Sys. v. Betts,* 492 U.S. 158, 171, 109 S.Ct. 2854, 106 L.Ed.2d 134 (1989). As discussed above, this broader definition would upset the careful balance that requires a full resolution of the potential infringement issues involved in overlapping patented and unpatented uses.

The legislative history does not add any clarity to the meaning of "patent information." During the floor debate, Senators occasionally referred to the need to correct "patent information." *See, e.g.,* 149 Cong. Rec. S15746 (daily ed. Nov. 24, 2003) (statement of Sen. Schumer) (The counterclaim provision may "delist the patent or correct the patent information in FDA's Orange Book."). This court must read these statements to use the term "patent information" consistent with the express statutory definition. Accordingly, to preserve the Act's careful balance and to enforce the language of the statute, the explicit definition of "the patent information" as "the patent number and the expiration date" controls.

VI.

[6] Caraco argues that in case this court does not find that Caraco is entitled to a counterclaim, this court should affirm the district court's injunction under the doctrine of patent misuse. Because the judicial doctrine of patent misuse creates an unusual circumstance where an infringer can escape the consequences of its infringing conduct because the victim of that tort may have used its patent rights to gain an unfair competitive advantage against an unrelated third party, this court examines such allegations with particularity. *See, e.g., C.R. Bard v. M3 Sys.,* 157 F.3d 1340, 1372-73 (Fed.Cir.1998) ("Although the law should not condone wrongful commercial activity, the body of misuse law and precedent need not be enlarged into an open-ended pitfall for patent-supported commerce."). For instance, the doctrine may apply where the patentee's misconduct toward unrelated parties amounted to unfair market benefits beyond the scope of the patent. *See Mallinckrodt, Inc. v. Medipart, Inc.,* 976 F.2d 700, 704 (Fed.Cir.1992) . In any event, in this case, the district court, apparently recognizing the rarity of this situation, expressly declined to address the doctrine of patent misuse. Without any finding to review, this court declines to adjudicate this issue in the first instance. *See Ecolab, Inc. v. FMC Corp.,* 569 F.3d 1335, 1352 (Fed.Cir.2009).

VII.

This court therefore reverses the district court's grant of summary judgment on Caraco's attempted, but unsuccessful, counterclaim and vacates the injunction ordering Novo to correct its use code for the '358 patent listed in the Orange Book for PRANDIN.

REVERSED and *VACATED.*

CLEVENGER, Circuit Judge, concurring.

I agree with Judge Rader's analysis of the relevant statutory provisions in this case and therefore join the opinion he writes for the court. I am not as certain as Judge Rader that the ongoing Paragraph IV litigation will cleanly resolve the dispute between the parties.

The dissent masks the cause for the dispute between the parties. Novo did nothing that was illegal or forbidden. FDA voluntarily requested a change to the approved indications for PRANDIN® which required Novo to use FDA's new approved labeling. The change also permitted Novo to revise its use code as the relevant FDA form, "Patent Information Submitted Upon and After Approval of an NDA or Supplement," expressly instructed Novo to "[s]ubmit the description of the approved indication or method of use that ***1368** you propose FDA include as the 'Use Code' in the Orange Book." Novo changed its use code to match the new PRANDIN® indication. Nothing in the record suggests that Novo is responsible for the labeling change, which, given the statutory and regulatory framework, happens to benefit Novo at Caraco's expense.

If not for FDA's request that Novo change its labeling to the present broad indication, everything would have worked properly under the relevant statutes. As Judge Rader notes, the "efficient dispute resolution mechanism" was in play. Caraco filed its ANDA for repaglinide, and by making its Paragraph IV certification had committed the statutory act of infringement. Novo followed with its infringement suit. Caraco was prepared to defend on the grounds that its proposed use of repaglinide would not induce infringement of the '358 patent. Caraco also filed a section viii statement in light of the then-approved labeling and use code for PRANDIN®, and proposed carve-out language in its labeling to signify its proposed noninfringing use of repaglinide. Caraco was thus set to get FDA approval to bring its generic drug to market and to defend itself in Novo's Paragraph IV suit.

But FDA, acting independently, gummed up the works. By requiring a single broad indication for repaglinide as part of the approved labeling, FDA created a situation where Caraco can no longer assert that its proposed labeling does not infringe the '358 patent. It remains to be seen what impact FDA's action will have on Caraco's ability to defend itself in the ongoing Paragraph IV litigation, but FDA's regulatory action threatens to impair Caraco's ability to disprove infringement. FDA thus may have inadvertently upset the careful balance of interests represented by the efficient dispute resolution mechanism Congress created in the Hatch-Waxman Act.

The dissent's fix would be to have United States District Courts dictate to FDA what indications should be used on the prescribed labeling for approved drugs, even though there is nothing illegal, or even incorrect, about Novo's current use code. There is no basis for a counterclaim to correct or delete the patent information submitted by Novo. If a fix is in order under the circumstances of this case, it lies with the FDA and Congress to understand the consequences of changing the approved repaglinide labeling to a single broad indication, and corresponding use code, and to remedy the situation. Laying blame on Novo is wrong.

The counterclaim statute, which the dissent would expand beyond its literal reach, was designed to cure the situation presented in *Mylan.* Congress has not addressed the fact situation presented in this case. Congress is the appropriate entity to readjust, if necessary, the delicate balance it has struck between original drug manufacturers and their generic counterparts.

DYK, Circuit Judge, dissenting.

In 2003, Congress enacted the counterclaim provision of the Hatch-Waxman Act in order to prevent manipulative practices by patent holders with respect to the Orange Book listings. These practices were designed to delay the onset of competition from generic drug manufacturers. *See* Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub.L. No. 108-173, § 1101(a)(2)(C), 117 Stat.2066, 2452 (codified at 21 U.S.C. § 355(j)(5)(C)(ii)) ("the counterclaim amendment"). In my view, the majority, in reversing the district court, now construes the statute contrary to its manifest purpose and allows the same manipulative practices to continue in the context of method patents. The amendment was designed to permit the courts to order correction***1369** of information published in the Or-

ange Book, yet under the majority's opinion, erroneous Orange Book method of use information cannot be corrected. I respectfully dissent.

I

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act, commonly known as the "Hatch-Waxman Act." Pub.L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. § 355 and scattered sections of 35 U.S.C.). Under the Hatch-Waxman Act, Congress required the Food and Drug Administration ("FDA") to maintain and publish a list of patents associated with approved drugs and methods of use. *See id.* § 102(a)(1). The FDA has implemented this provision by publishing this list in its publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"). *See* 21 C.F.R. § 314.53(c)(2)(i)(O).[FN1] The statute is complicated, but its operation in the present context is not.

FN1. *See also* Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying that a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 68 Fed.Reg. 36,676, 36,686 (June 18, 2003) (codified at 21 C.F.R. pt. 314) ("Report and Order Accompanying the Patent Listing Rule").

A

Under the Food, Drug, and Cosmetic Act ("FDCA"), a drug manufacturer must secure approval from the FDA for the sale of any drug in interstate commerce. 21 U.S.C. § 355(a). To do so, the manufacturer files a New Drug Application ("NDA") with the FDA to secure approval for a "new drug," 21 U.S.C. § 355(b)(1) , a term which encompasses a new use for an existing drug, *see* 21 C.F.R. § 310.3(h)(4). The application requires that the manufacturer specify the drug (or drugs) in question and the proposed method (or methods) of use. *See* 21 C.F.R. § 314.53(b)-(c). The drug cannot be sold until the FDA has approved the drug for the particular method of use, 21 U.S.C. § 355(a), (b)(1), and the method of use is required to appear on the label, 21 U.S.C. § 352(f); 21 C.F.R. pt. 201, *id.* § 314.125(b)(8). Section 355(b) also requires the NDA filer to list all patents "with respect to which a claim of patent infringement could reasonably be asserted" by patent number and expiration date with its NDA application, 21 U.S.C. § 355(b)(1), while section 355(c)(2) requires NDA applicants to provide the same information with respect to patents issuing after the NDA application was approved, *id.* § 355(c)(2). This information, referred to as "information submitted ... under subsection (b) or (c)" or "patent information," is published in the Orange Book. *Id.* § 355(b)(1), (c)(2).

A generic manufacturer may piggyback on the safety and efficacy data the original drug manufacturer submitted in its NDA, and may seek approval for an identical method of use for its identical generic product by submitting an "Abbreviated New Drug Application," or "ANDA." *See id.* § 355(j). If a patent is listed in the Orange Book for a drug or method of use covered by the NDA, the generic is generally required to certify that the patent has expired or is invalid or will not be infringed by the sale or use of the drug for which the ANDA is submitted. *Id.* § 355(j)(2)(A)(vii). In what is called a "paragraph IV" certification regarding noninfringement and invalidity, approval is stayed pending the outcome of court litigation to determine infringement and validity.[FN2] Recognizing that some NDAs would ***1370** cover both uses covered by a patent and uses not covered by a patent, Congress enacted "section viii," which allows the ANDA applicant to limit its application to unpatented uses, and to secure approval for those unpatented uses. *Id.* § 355(j)(2)(A)(viii); H.R. Rep. No. 98-857 pt. 1, at 22 (1984), *as reprinted in* 1984 U.S.C.C.A.N. 2647, 2655.

FN2. Where the applicant makes this paragraph IV certification, the patentee has forty-five days to bring suit for infringement of the patent that is the subject of the generic manufacturer's certification, and the approval of the ANDA is stayed for a period of thirty-months (or until the resolution of the infringement suit, whichever is shorter). *See* 21 U.S.C. § 355(j)(5)(B)(iii). The first ANDA applicant to

> make a paragraph IV certification benefits from a 180-day period of marketing exclusivity, *id.* § 355(j)(5)(B)(iii)(IV)(iv), a provision intended encourage generic manufacturers to undertake challenges to patents claimed to cover brand drugs. *See Teva Pharms. USA, Inc. v. Sebelius,* 595 F.3d 1303, 1318 (D.C.Cir.2010).

Some NDA filers realized that they could block generic competition by making unwarranted claims to patent coverage, for example, by listing in the Orange Book a patent for a drug or method of use when in fact the patent was clearly inapplicable. The FDA repeatedly declined to police the Orange Book listings,[FN3] and before the enactment of the counterclaim provision in 2003, we held that the courts could not do so through declaratory judgments. *See Mylan Pharms., Inc. v. Thompson,* 268 F.3d 1323, 1332-33 (Fed.Cir.2001).

> FN3. The FDA has consistently held the position that its role in listing patents in the Orange Book is "ministerial," and that establishing an administrative process for reviewing patents, assessing patent challenges, and de-listing patents would involve patent law issues that are beyond its expertise and authority. *See, e.g.,* Report and Order Accompanying the Patent Listing Rule, 68 Fed.Reg. at 36,683.

Congress responded by enacting the counterclaim amendment as part of the "Greater Access to Affordable Pharmaceuticals Act" ("Gregg-Schumer Bill"), enacted in 2003. S. 1225, 108th Cong. (2003). The counterclaim amendment provides:

> (ii) Counterclaim to infringement action.-
>
> (I) In general.-If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent *or a use of which is claimed by the patent* brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to *correct or delete the patent information submitted by the holder under subsection (b) or (c) of this section* on the ground that the patent does not claim either-
>
> (aa) the drug for which the application was approved; or
>
> (bb) *an approved method of using the drug.*

21 U.S.C. § 355(j)(5)(C)(ii) (emphases added). Thus, the amendment allows an ANDA applicant, who is defending against a patent infringement suit brought by the holder of the NDA, to assert a counterclaim to correct or delete the Orange Book "patent information submitted ... under subsection (b) or (c)" on the ground that the patent does not claim "the drug for which the application was approved" or "an approved method of using the drug." We have not previously construed this provision. The majority now holds that the counterclaim provision is unavailable to correct erroneous method of use information in the Orange Book-on two separate grounds.

II

A

In my view, the majority has misconstrued the term "patent information submitted***1371** ... under subsection (b) or (c)." *Id.* § 355(j)(5)(C)(ii)(I). In the majority's view, method of use information is not "patent information." The majority construes the term as limited to the patent number and expiration date: "[T]he Act defined the term 'patent information' as 'the patent number and the expiration date.' " Majority Op. at 1366. There is, in fact, no definition of "patent information" in the statute, and in reaching this construction, the majority ignores critical statutory language. The statute requires the NDA applicant to

> file with the application the patent number and the expiration date of any patent *which claims the drug for which the applicant submitted the application* or *which claims a method of using such drug* and *with respect to which a claim of patent infringement could reasonably be asserted* if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

21 U.S.C. § 355(b)(1) (emphases added). Thus, the

statute requires the NDA applicant to list patents claiming a drug or method of use "with respect to which a claim of patent infringement could reasonably be asserted." In other words, the statute on its face contemplates that the scope of the patent must be accurately described and that the patent must be related to the drug or method of use for which the NDA application is submitted. FN4 The statute does not require the listing of patent numbers and expiration dates in the abstract. It contemplates the description of the scope of the patent and of the relationship between the patent and the drug or the method of use; the description of that scope and relationship is itself "patent information." The statute requires that this information be published, stating that the Secretary "shall publish information submitted under the two preceding sentences." *Id.*

> FN4. Subsection (b) refers to patent information submitted with an NDA application; subsection (c) describes the requirements for the submission of patent information after an NDA has already been filed. The patent listing and publication requirements of 21 U.S.C. § 355(c)(2) parallel those in § 355(b)(1):
>
> > If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.... Upon the submission of patent information under this subsection, the Secretary shall publish it.

Other provisions of the statute also contemplate that the ANDA filer will be able to understand the scope of the patent and to *relate* the patent information to the drug or drugs being claimed and the method or methods of use being claimed. *See id.* § 355(b)(1). Describing the scope of the patent and relating the listed patents to the drug or method of use is essential to the operation of the statute, as the basic idea of the patent listings in the Orange Book is to put ANDA applicants on notice regarding which listed drugs and methods of use may be copied and which drugs or method of use are patent protected, and to enable the ANDA filer to submit an appropriate certification as required by law. The statute requires an ANDA applicant to provide, as part of the application,

> (vii) a certification, in the opinion of the applicant and to the best of his knowledge, *with respect to each patent* ****1372*** *which claims the listed drug* referred to in clause (i) or *which claims a use for such listed drug for which the applicant is seeking approval* under this subsection and *for which information is required to be filed under subsection (b) or (c) of this section-*
>
> (I) that such patent information has not been filed,
>
> (II) that such patent has expired,
>
> (III) of the date on which such patent will expire, or
>
> (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted....

Id. § 355(j)(2)(A)(vii) (emphases added). Similarly, the section viii certification provision also appears to contemplate that information submitted under subsection (b) or (c) will encompass information regarding the patented method of use. The statute directs the ANDA applicant to submit,

> if with respect to the listed drug referred to in clause (i) *information was filed under subsection (b) or (c) of this section for a method of use patent* which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

Id. § 355(j)(2)(A)(viii). The statute plainly contemplates that "patent information" will include information that describes the scope of the patent and that relates the patent to the drug or method of use.

B

Quite apart from the fact that the majority's limiting interpretation is inconsistent with the statutory language and structure, the majority's interpretation is in my view untenable for other reasons.

First, the majority agrees that the counterclaim amendment was designed to overrule our decision in *Mylan.* Majority Op. at 1365. In overruling *Mylan,* Congress viewed erroneous information as to the scope of the patent and its relationship to an approved drug or method of use as "patent information" that could be ordered corrected. The majority appears to suggest that the overruling of *Mylan* is limited to the precise facts of *Mylan,* namely, the situation in which correction of the error would require that the patent number be deleted entirely from the Orange Book. See *id.* The overruling would not apply to a situation in which other erroneous Orange Book information is involved, for example, where the patent is erroneously listed with respect to a particular drug or method of use, but is properly listed elsewhere in the Orange Book. This ignores the context of the *Mylan* decision.

The first thing to understand is that the majority's description of the Orange Book likely bears no relationship to the actual document. The Orange Book is not a list of patents from which a particular patent could be excised. The Orange Book is a list of NDAs that associates particular patents with approved drugs or methods of use. Correction of an Orange Book listing does not strike a patent from a list, it strikes (or corrects) the listing that associates the patent with a particular NDA, approved drug, or method of use.

The problem in *Mylan* was that the Orange Book improperly described the scope of the patent and improperly related the patent to a drug and method of use not covered by the patent. In *Mylan,* Bristol-Myers Squibb ("Bristol") owned U.S. Patent No. 4,182,763 ("the '763 patent") directed to the treatment of anxiety through the administration of buspirone hydrochloride. 268 F.3d at 1327. The '763 patent was listed in the Orange Book in connection with that use but was about to expire. *Id.* Eleven hours before the patent's expiration, Bristol delivered to the FDA copies of U.S. Patent No. 6,150,365 (the "'365 patent"), which included a single method ***1373** claim directed to the treatment of anxiety using a "metabolite" of buspirone.[FN5] *Id.* at 1327-28. Bristol sought to have the '365 patent listed in the Orange Book as covering buspirone and a method of using buspirone. *Id.* at 1328. Mylan and other ANDA applicants challenged the listing of the '365 patent on the ground that it only covered a metabolite of buspirone, and a method of using a metabolite of buspirone to treat anxiety. *Id.* After the FDA refused to correct the listing, Mylan filed suit for a declaratory judgment that Bristol improperly listed the '365 patent in the Orange Book as covering buspirone and the use of buspirone, and a preliminary injunction requiring Bristol to delist the '365 patent. *Id.* Reversing the district court, we held that there was no declaratory relief available to correct an erroneous Orange Book listing. *Id.* at 1332-33.

> FN5. A metabolite is "[a] product of intermediary metabolism." *McGraw-Hill Dictionary of Scientific and Technical Terms* 1319 (6th ed.2003). We held in *Hoechst-Roussel Pharms., Inc. v. Lehman,* 109 F.3d 756, 759 (1997), that a patent claiming either the active ingredient of a drug or a method of using that ingredient does not also cover metabolites of that ingredient.

Thus, in *Mylan,* the accused infringer challenged the accuracy of the listing associating the patent with the approved method of use. Congress acted to provide a counterclaim action to correct such errors. Congress' concern with the proper listing of the patent in the Orange Book does not remotely suggest a myopic congressional focus on situations where the patent belonged nowhere in the Orange Book, as the majority suggests. Most significantly, viewing the overruling of *Mylan* as limited to complete delisting would be inconsistent with the explicit statutory language, which provides for correction of Orange Book information "on the ground that

the patent does not claim ... the drug for which the application was approved." 21 U.S.C. § 355(j)(5)(C)(ii)(I). The statute thus must allow correction of a misdescription of patent scope that includes a drug not covered by the patent and erroneous information about the relationship between the patent and the drug, even if the patent is properly listed elsewhere in the Orange Book. In other words the scope of the patent and its relationship to the drug must be "patent information."

Moreover, if "patent information" includes information as to the scope of the patent with respect to the drug and the relationship between the patent number and the drug, it must also include Orange Book information describing the scope of a method of use patent and linking the method of use to the patent. There is no basis in the statutory language or statutory purpose for distinguishing between drug information and method of use information. Either both must be "patent information," or neither must be patent information. In my view, all Orange Book information is "patent information."

Second, at the time the counterclaim provision was enacted in 2003, the FDA had adopted the Patent Listing Rule,[FN6] making clear that the agency had adopted a broad interpretation of "patent information submitted ... under subsection (b) or (c)." That interpretation is entitled to *Chevron* deference even if the language of the statute is ambiguous, and not (as I urge) plainly contrary to the majority's interpretation. *See Chevron U.S.A. Inc. v. Natural Res. Def. Council,* 467 U.S. 837, 843-44, 104 S.Ct. 2778, 81 L.Ed.2d 694 (1984). By the time of the counterclaim ***1374** amendment in 2003, the FDA had adopted detailed requirements for the submission of "patent information" for both drugs and methods. The 2003 rule, published as a proposed rule in the *Federal Register* in late 2002 [FN7] and finalized six months before the counterclaim amendment, includes a section entitled "Submission of patent information" on the requirements for the listing of a patent in the Orange Book. *See* 21 C.F.R. § 314.53. The report accompanying the regulatory revision makes clear that the FDA is defining what constitutes "patent information" for purposes of subsections (b) and (c).[FN8] Additionally, the report accompanying the Proposed Rule in 2002 confirms that the FDA's authority for the 2003 rule arises from not only the FDA's general authority to enforce the FDCA under 21 U.S.C. § 371, but also its authority to implement section 505 of the Hatch-Waxman Act, "including the patent listing and patent certification requirements" in section 505(b). *See* Proposed Rule, 67 Fed.Reg. at 65,457. The regulation itself provides that "patent information" includes 1) "[i]nformation on the drug substance (active ingredient) patent including ... [w]hether the patent claims the drug substance that is the active ingredient in the drug product described in the new drug application or supplement," 2) "[i]nformation on the drug product (composition/formulation) patent including ... [w]hether the patent claims the drug product for which approval is being sought," [FN9] and 3) "[i]nformation on each method-of-use patent including ... [w]hether the patent claims one or more methods of using the drug product for which approval is being sought and a description of each pending method of use or related indication and related patent claim of the patent being submitted." [FN10]

FN6. The full title of the final rule was: "Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying that a Patent Claiming a Drug Is Invalid or Will Not Be Infringed," 68 Fed.Reg. 36,676.

FN7. *See* Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying that a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 67 Fed.Reg. 65,448 (Oct. 24, 2002) ("Proposed Rule").

FN8. The Report explains why it is promulgating the regulation, and in fact this is because of the existence of subsections (b) and (c):

To explain why we (FDA) issued the propos-

> al, we first describe how Federal law requires NDA applicants to file patent information and how that patent information can affect the approval of ANDA and 505(b)(2) applications....
>
> Section 505(b)(1) of the act (21 U.S.C. 355(b)(1)) requires all NDA applicants to file, as part of the NDA, "the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." Section 505(c)(2) of the act (21 U.S.C. 355(c)(2)) imposes a similar patent submission obligation on holders of approved NDAs when the NDA holder could not have submitted the patent information with its application.
>
> Under section 505(b)(1) of the act, we publish patent information after approval of an NDA application in our approved drug products list entitled "Approved Drug Products With Therapeutic Equivalence Evaluations." This list is known popularly as the "Orange Book" because of its orange-colored cover. If patent information is submitted after NDA approval, section 505(c)(2) of the act directs us to publish the information upon its submission.
>
> Report and Order Accompanying the Patent Listing Rule, 68 Fed.Reg. at 36676.

FN9. A "drug product" is a "finished dosage form ... that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients." *See* 21 C.F.R. § 314.3. A "drug substance" is "an active ingredient that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body." *Id.*

FN10. These listing requirements are described in 21 C.F.R. § 314.53(c)(2), while § 314.53(c)(1) provides: "An [NDA] applicant ... shall submit the required patent information described in paragraph (c)(2) of this section for each patent that meets the requirements described in paragraph (b) of this section."

***1375** The NDA applicant is thus not only required to submit the patent number and the expiration date as part of its application, but is also required to describe the scope of the patent and *relate* the drug substance, drug product, or method of use in question to the particular patent. Furthermore, the regulation requires an NDA holder or applicant to complete FDA Form 3542, which requires the applicant to identify whether the submitted patent claims a "drug substance," "drug product," or "method of use," and link such information to each patent for which information is being submitted. *See* J.A. 918-20. The information in this form provides the basis for the Orange Book listing. *See* 21 C.F.R. § 314.53(c)(2)(ii).

Congress was well aware of this regulatory interpretation of "patent information" when it enacted the counterclaim provision. As Senator Schumer, one of the original sponsors of the amendment, stated, "The bill provides a *critical complement to the work the FDA has done in clarifying its regulations on patent listing,* but it goes much further." *Legislative and Regulatory Responses to the FTC Study on Barriers to Entry in the Pharmaceutical Marketplace: Hearing Before the S. Comm. on the Judiciary,* 108th Cong. 19 (2003) (emphasis added). Additionally, in several places in the legislative history the FDA regulation is cited approvingly. *See* 149 Cong. Rec. S8690 (daily ed. June 26, 2003) (statement of Sen. Hatch, then-chairman of the Senate Committee on the Judiciary); 149 Cong. Rec. S8197 (daily ed. June 19, 2003) (statement of Sen. Frist, then Senate Majority Leader).

Quite apart from *Chevron,* it is well established that where, as here, Congress was specifically aware of the

agency's interpretation of a statutory term at the time the statute was enacted, this is compelling evidence of legislative adoption of the agency's interpretation. This principle has been recognized by the Supreme Court for decades, both in the context of reenactment of existing statutes where statutory terminology had been construed by the agency before the reenactment,[FN11] and in the context of new legislation utilizing terminology that the agency had previously construed.[FN12] Here, Congress utilized the FDA's interpretation of "patent information" by enacting the Gregg-Schumer Bill with full awareness of the agency's interpretation of the term, and the FDA's interpretation is binding on us in construing the statute.

FN11. *See United States v. Bd. of Comm'rs of Sheffield, Ala.,* 435 U.S. 110, 131-35, 98 S.Ct. 965, 55 L.Ed.2d 148 (1978) (adopting the Attorney General's interpretation of "state[s] and political subdivision" to include all political units in a designated jurisdiction where Congress was aware of the Attorney General's interpretation when it reenacted the Voting Rights Act without change in 1975); *Cammarano v. United States,* 358 U.S. 498, 510, 79 S.Ct. 524, 3 L.Ed.2d 462 (1959) (adopting IRS' construction of "ordinary and necessary" business expenses as excluding sums spent to persuade the public of the desirability of proposed legislation affecting the taxpayer's business, as Congress reenacted the Internal Revenue Code without substantive change to the business expense deduction); *Hartley v. Comm'r,* 295 U.S. 216, 220, 55 S.Ct. 756, 79 L.Ed. 1399 (1935) (adopting IRS' construction of "basis" for the purposes of a decedent's estate to be the property's value at the time of decedent's death, as Congress reenacted the pertinent Internal Revenue Code provisions without substantive change).

FN12. *See Traynor v. Turnage,* 485 U.S. 535, 546, 108 S.Ct. 1372, 99 L.Ed.2d 618 (1988) (adopting Veterans' Administration's construction of "willful misconduct" as including alcoholism, where Congress enacted GI Bill using the same "willful misconduct" language previously construed by the Veterans' Administration).

***1376** Third, the legislative history makes clear that Congress was concerned with correcting Orange Book information generally. The legislative history suggests a broad concern with preventing brand manufacturers from manipulating the patent listing system in the Orange Book in order to delay entry of generics into the market. *See* 149 Cong. Rec. 31,200 (2003) (statement of Sen. Schumer) ("The [new] provisions close loopholes in the law and end the abusive practices in the pharmaceutical industry which have kept lower-priced generics off the market and cost consumers billions of dollars.").[FN13] The purpose of the statutory provision as reflected in the legislative history refers broadly to correction of Orange Book information, not just to correction of patent numbers and expiration dates. As Senator Schumer described it, "[T]he provisions enforce *the patent listing requirements at the FDA* by allowing a generic applicant, when it has been sued for patent infringement, to file a counterclaim to have the brand drug company *delist the patent* or *correct the patent information in the FDA's Orange Book.*" 149 Cong. Rec. S15,746 (daily ed. Nov. 24, 2003) (emphases added).

FN13. *See also* 149 Cong. Rec. at S8191 (daily ed. June 19, 2003) (statement of Sen. Schumer) ("A lot of blockbuster drugs were on the market. Their patents were about to expire. The drug industry ... came to the conclusion that they had to do everything they could, they had to pull out all the stops to extend their monopolies. They came up with wild and crazy schemes to do it, such as patenting the substance the body makes when the drug is ingested; developing computer programs and listing the patents on the drug; and, in one case, absurdly, a new patent was asked for because the color of the bottle was changed. That was never the concept of Hatch-Waxman.").

Under the circumstances, it seems to me that we must interpret the phrase "patent information submitted ... under subsection (b) or (c)" to include Orange Book

information that describes the scope of the patent and relates the patent number and expiration date to the drug or method of use and, in particular, that "patent information" submitted under subsections (b) and (c) must be interpreted to include the patent information required by the 2003 regulation, including method of use information.

III

In my view, the majority also errs by interpreting "an approved method of using the drug" in 21 U.S.C. § 355(j)(5)(C)(ii)(I)(bb) to mean "any" approved method of use approved in the patentee's NDA. The majority's approach here is fundamentally inconsistent with the Supreme Court's admonition, in a recent opinion by Justice Scalia, that "[u]ltimately context determines meaning," *Johnson v. United States,* --- U.S. ----, 130 S.Ct. 1265, 1270, 176 L.Ed.2d 1 (2010), and the Court's repeated instruction that "[i]n expounding a statute, we must not be guided by a single sentence or member of a sentence, but look to the provisions of the whole law, and to its object and policy," *U.S. Nat'l Bank of Or. v. Indep. Ins. Agents of Am., Inc.,* 508 U.S. 439, 455, 113 S.Ct. 2173, 124 L.Ed.2d 402 (1993) (quoting *United States v. Heirs of Boisdoré,* 49 U.S. (8 How.) 113, 122, 12 L.Ed. 1009 (1849)).

The evident purpose of the counterclaim provision is to allow for the correction of "patent information submitted ... under (b) or (c)." In other words, as discussed above, the provision is designed to provide for correction of erroneous Orange Book information submitted by the NDA applicant or holder, including information with respect to patent coverage of both drugs and methods of use. That purpose is reflected in the language of the statute, which allows an ANDA applicant defending against an infringement action to "assert***1377** a counterclaim seeking an order requiring the [NDA] holder *to correct or delete the patent information submitted by the holder* under subsection (b) or (c) of this section *on the ground that the patent does not claim either(aa) the drug for which the application was approved; or (bb) an approved method of using the drug.*" 21 U.S.C. § 355(j)(5)(C)(ii)(I) (emphases added). In other words, if the submitted Orange Book information claims patent coverage for an approved drug not covered by the patent or a method of use not covered by the patent, that information may be corrected.

Thus, the reference to "an approved method of using the drug" in subsection (bb) must refer to *information in the Orange Book* concerning "an approved method of using the drug." The majority's error lies in focusing on the relationship between the patent and the NDA (which is not Orange Book information), rather than the relationship between the patent and the Orange Book listing. Under the majority's view, no correction of erroneous Orange Book information is permitted so long as the patent covered *any* approved method of use covered by the NDA. The patent can be listed in the Orange Book as erroneously covering approved use A, despite the fact that the patent actually covers approved use B, and the counterclaim provision provides no mechanism for correction. This cannot be what Congress intended. FN14

> FN14. The majority suggests that Congress borrowed the statutory language from our decision in *Mylan* and that this shows that "an" means "any," because in *Mylan* the patent did not relate to any approved use. Majority Op. at 1365. I have demonstrated above that Congress could not have intended to limit the counterclaim provision to the particular facts in *Mylan.*

Moreover, the statutory language referring to "an approved method of using the drug" obviously refers, once again, to the terminology used in the 2003 Patent Listing Rule. That regulation required that for "each method of use patent" the NDA applicant submit certain information, including "[w]hether the patent claims one or more approved methods of using the approved drug product and a description of *each approved method of use or indication and related patent claim of the patent being submitted.*" 21 C.F.R. § 314.53(c)(2)(ii)(P)(1) (emphasis added). In other words, the regulation requires the patentee to *relate* the patent to the approved method of use. Subsection (bb) is directly concerned with correction of the Orange Book patent information relating the patent to the approved method of use.

Once the overall operation of the statutory scheme is understood, the text is clear. *Webster's Third New International Dictionary* describes "a" as being "used as a function word before a singular noun followed by a restrictive clause or other identifying modifier <*a man who was here yesterday* >." *Webster's Third New International Dictionary* 1 (2002) (emphasis added). This definition appears *before* the definition of "a" as "any." *See id.* As the example illustrates, "an" in this case may be the function word before the singular noun ("approved method of using the drug") conveying a particular identity through the use of a restrictive clause. The restrictive clause here is implicit-"an approved method of using the drug" logically refers to an approved method of use listed by the NDA holder in the Orange Book, as associated with the listed patent. Thus, "an" refers to a particular method of using the drug, that is, the particular approved method listed by the NDA holder in the Orange Book. This is the only interpretation of the statutory language that yields a result that is not plainly at variance with the purpose of the legislation as ***1378** a whole. *See Nixon v. Mo. Mun. League,* 541 U.S. 125, 138, 124 S.Ct. 1555, 158 L.Ed.2d 291 (2004) (citing *United States v. Am. Trucking Ass'n,* 310 U.S. 534, 543, 60 S.Ct. 1059, 84 L.Ed. 1345 (1940)). "As in all cases of statutory construction, our task is to interpret the words of these statutes in light of the purposes Congress sought to serve." *Chapman v. Houston Welfare Rights Org.,* 441 U.S. 600, 608, 99 S.Ct. 1905, 60 L.Ed.2d 508 (1979).

In short, the statute must be construed to read as follows:

> (ii) Counterclaim to infringement action.-
>
> (I) In general.-If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) of this section on the ground that the patent does not claim either-
>
> (aa) the [associated] drug for which the application was approved; or
>
> (bb) an [associated] approved method of using the drug.

An error in an Orange Book use code, which covers an unpatented method of use, is subject to correction under a proper reading of the counterclaim provision.

IV

The facts in this case well illustrate the true manipulation that the counterclaim provision was designed to avoid. Here Novo Nordisk ("Novo") was originally the owner of the patent on the chemical composition of repaglinide, U.S. Patent No. RE37,035 ("the '035 patent") , which expired on March 14, 2009. *See Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.,* 656 F.Supp.2d 729, 730 (E.D.Mich.2009). Novo is also the owner of a patent covering the use of repaglinide in monotherapy to treat diabetes, U.S. Patent No. 5,312,924 ("the '924 patent"), which expired in September of 2006. The expiration of these patents meant that Novo could not claim any patent protection for monotherapy use of PRANDIN. However, Novo acquired an additional patent in 2004 (the patent in suit) claiming 1) a chemical composition of repaglinide and metformin; and 2) a method for treating non-insulin dependent diabetes mellitus (NIDDM) comprising administering to a patient repaglinide in combination with metformin. *See* U.S. Patent No. 6,677,358 col.10 ll.42-43, 48-51 ("the '358 patent"). The '358 patent is not set to expire until June 12, 2018.

Following issuance of the '358 patent on January 13, 2004, Novo submitted an FDA Form 3546, dated February 5, 2004, associated with NDA 020741 (for PRANDIN). *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.,* 649 F.Supp.2d 661, 663 (E.D.Mich.2009). The use code narrative was limited to claiming a use of PRANDIN in combination therapy. It read: "U-546-USE OF REPAGLINIDE IN COMBINATION WITH METFORMIN TO LOWER BLOOD GLUCOSE." *Id.* at 664. Thus, the Orange Book entry in 2004 included the following:

APPL/PROD NUMBER	INGREDIENT NAME; TRADE NAME	PATENT NUMBER	PATENT/PED EXCL EXPIRES	PATENT CODE(S)
020741 001	REPAGLINIDE; PRANDIN	6677358	JUN 12, 2018	DS DP U546
020741 002	REPAGLINIDE; PRANDIN	6677358	JUN 12, 2018	DS DP U546
020741 003	REPAGLINIDE; PRANDIN	6677358	JUN 12, 2018	DS DP U546

***1379** *See* J.A. 1235.

Caraco Pharmaceutical Laboratories, Limited ("Caraco") filed an ANDA seeking approval to market repaglinide for the treatment of diabetes in anticipation of the expiration of the '035 patent. *Novo Nordisk,* 649 F.Supp.2d at 662. In June 2005, Novo sued Caraco, claiming that if Caraco marketed repaglinide, it would infringe. Complaint at 3, *Novo Nordisk,* 649 F.Supp.2d 661.[FN15] Novo did not claim that Caraco would infringe the '924 patent or the '035 patent; nor could Novo make such a claim since Caraco sought approval to market repaglinide only after both patents expired. Rather, Novo claimed that Caraco would induce infringement of the '358 patent, apparently because the Caraco label would suggest the use of repaglinide together with metformin.

FN15. In particular, Novo asserted that marketing of repaglinide would infringe claim 4 of the '358 patent, which claimed:

> A method for treating non-insulin dependent diabetes mellitus (NIDDM) comprising administering to a patient in need of such treatment repaglinide in combination with metformin.
>
> '358 patent col. 10 ll.48-51.

Following the FDA's suggestion, Caraco sought a section viii certification, making clear that it was not seeking approval to market the use of repaglinide in combination with metformin (by limiting its label to the monotherapy use).[FN16] Based on the existing U546 use code description for PRANDIN (limiting the description of the patent to combination therapy), the FDA permitted Caraco to move forward with its label carving out information pertaining to use of repaglinide in combination with metformin. *See* J.A. 625-43.

FN16. Caraco initially made a paragraph IV certification with respect to Claim 4 of the '358 patent and a paragraph III certification with respect to the '035 patent on repaglinide. Opposition to Plaintiffs-Appellants' Emergency Motion to Stay Mandatory Injunction Pending Appeal at exh. 7, at 3, *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.,* No.2010-1001 (Fed.Cir. Oct. 7, 2009). However, at the FDA's urging it sought a "split certification," a paragraph IV certification as to the drug product claims of the '358 patent, and a section viii certification as to the method claim. *See* J.A. 635.

Several months later, Novo then broadened the use code for PRANDIN associated with the '358 patent, changing the use code to read: "U-968-A METHOD FOR IMPROVING GLYCEMIC CONTROL IN ADULTS WITH TYPE 2 DIABETES MELLITUS." *Novo Nordisk,* 649 F.Supp.2d at 664. The Orange Book listing for PRANDIN then included the following:

APPL/PROD NO	PATENT NO	PATENT EXPIRATION DATE	PATENT CODES
REPAGLINIDE-PRANDIN			

N020741 001	6677358	Jun 12, 2018	DS DP U-968
N020741 002	6677358	Jun 12, 2018	DS DP U-968
N020741 003	6677358	Jun 12, 2018	DS DP U-968

See U.S. Dep't of Health & Human Servs., *Approved Drug Products with Therapeutic Equivalence Evaluations* add. A, at 157 (30th ed.2010). Since U-968 appeared to encompass the use of repaglinide in monotherapy to treat diabetes, the FDA reversed itself and rejected Caraco's proposed labeling carve-out, requiring Caraco to include the information regarding the patented repaglinide-metformin combination therapy in its generic label.[FN17]

> FN17. With the exception of the carve-out to avoid the infringing use, the language of the generic label must otherwise match that of the original drug label. *See* 21 U.S.C. § 355(j)(2)(A)(v), (j)(4)(G); 21 C.F.R. § 314.94(a)(8)(iv). Thus, in this case, without the section viii carve-out, Caraco would be required to include information regarding the combination therapy included in PRANDIN's label (in the "Dosage and Administration" and "Clinical Pharmacology" sections) in its own label. *See* J.A. 637. The inclusion of information regarding the combination therapy would likely cause Caraco to induce infringement of the '358 patent.

***1380** Novo acknowledges that monotherapeutic use of repaglinide is *not* covered by the '358 patent. *See, e.g.,* Majority Op. at 1364 ("Novo and Caraco agree that the '358 patent claims only one of the three approved methods of using PRANDIN (i.e., repaglinide in combination with metformin)."). But the use code claims that the patent does cover the monotherapy use. In my view, this is precisely the type of situation that Congress intended the counterclaim provision to address.

The concurrence blames the FDA for Caraco's predicament, adopting Novo's disingenuous argument that the FDA, and not Novo, was responsible for the change in the use code. The concurrence accuses the FDA of "gumm[ing] up the works. By requiring a single broad indication for repaglinide as part of the approved labeling, FDA created a situation where Caraco can no longer assert that its proposed labeling does not infringe the '358 patent." Concurring Op. at 1368. First, the FDA did not require a change in the use code. The FDA does not interpret patents or police the Orange Book listings, the very source of the problem that led to the counterclaim provision. The FDA role in administering the Orange Book is ministerial: it simply lists the patent information that it receives from brand manufacturers, expecting those parties to abide by the statutory and regulatory mandates. *See Apotex, Inc. v. Thompson,* 347 F.3d 1335, 1349 (Fed.Cir.2003) (upholding the FDA's position that the FDA's duties with respect to the Orange Book are ministerial and that the Hatch-Waxman Act does not require the FDA to police the Orange Book listings to ensure compliance with regulatory and statutory requirements).

Second, while the FDA did require a general change in oral diabetes drug labeling in November of 2007 that required a corresponding change in the PRANDIN label, there is absolutely nothing in the statute or regulations that required Novo to change the use code to track this new indication.[FN18] The FDA did not direct or request that Novo change its use code to reflect the new indication, nor was Novo required under FDA regulations to make such a change. Indeed, in response to questioning at oral argument, Novo admitted this. Oral Arg. at 1:40-1:46 (" [The FDA directive of 2007] did not require [a change in the use code] ...").

> FN18. In November of 2007, as part of an ongoing reevaluation of the professional labeling of all oral antidiabetic drugs, the FDA required Novo to replace all separate indications with the following sentence: "PRANDIN is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus." *See* J.A. 667-68.

However, Novo argues that the labeling change re-

quired by the FDA in the "Indication" part of the label made the use code change appropriate. Novo argues that FDA Form 3542 allows them to submit either the method of use or the indication for the use code. Appellant's Br. 36 ("FDA's guidance is expressly written in the alternative: An applicant may describe *either* the indication *or* the method of use."). That is partially correct, FN19 but the form also requires that the use code information refer to that portion of the label ***1381** that relates to a patented use. *See* J.A. 919. An approved label, as in this case, may cover both patented uses and unpatented uses. Nothing in the FDA regulations or FDA Form 3542 suggests that the patentee may derive Orange Book use code information from that portion of the label referring to *unpatented* uses. Quite the contrary, the applicable regulations and FDA Form 3542 are clear that the patentee is required to utilize those portions of the label that refer to the *patented use. See* 21 C.F.R. § 314.53(c)(2)(ii)(P)(2) (requiring the NDA holder to identify "the specific section of the approved labeling for the drug product that corresponds to the method of use claimed by the patent submitted"); J.A. 919.

> FN19. The form provides alternatives with respect to submission of a proposed use code-it directs the NDA holder to "provide the information on the indication or method of use for the Orange Book." J.A. 920.

Here, the patentee did exactly what was expressly forbidden. For the proposed use code description submitted on the FDA Form 3542, Novo submitted the following: "A method for improving glycemic control in adults with type 2 diabetes mellitus." J.A. 673. It thus utilized that portion of PRANDIN's label that refers to the use of repaglinide standing alone to treat diabetes (an unpatented use), not to the use of repaglinide together with metformin (a patented use). FN20 There is no justification for using a portion of the label referring to an unpatented use to describe a patented use.

> FN20. Various other parts of the current PRANDIN label reference the combination therapy, such as the "Clinical Pharmacology" and "Dosage and Administration" sections of the label.

The manipulative nature of Novo's actions is confirmed not only by the lack of justification for the change, but also by the timing of the change (two years after the labeling change was initiated by the FDA and immediately after the FDA approved Caraco's section viii carve-out), and by its own admission that preventing approval of Caraco's ANDA was part of the motivation for changing the use code. At oral argument, Novo conceded that the decision to change the use code was in part "a response to the section viii ruling ... in December '08 from FDA." Oral Arg. at 3:43-4:03.

V

Finally, the majority opinion suggests that the court's restrictive interpretation of the counterclaim provision is not so bad because it does not leave Caraco without a remedy to correct the erroneous Orange Book listing. The majority is sanguine about the outcome, believing that forcing Caraco to defend the paragraph IV infringement suit will "facilitate[ ] efficient resolution of disputes concerning potential overlapping of protected and unprotected uses." Majority Op. at 1365. In contrast, the concurrence doubts that there is a remedy in the infringement suit, and I agree. As the concurrence notes, "[b]y requiring a single broad indication for repaglinide as part of the approved labeling, FDA created a situation where Caraco can no longer assert that its proposed labeling does not infringe the '358 patent." Concurring Op. at 1368. Indeed, Novo's adoption of a broad use code for PRANDIN likely prevents Caraco from being able to disprove infringement in the paragraph IV lawsuit, because Caraco is now compelled to include information regarding the patented combination therapy in its label.

Nor would there be a remedy in a suit under the Administrative Procedure Act ("APA"). To be sure, we have held that an APA action could be brought to challenge FDA action in refusing to police use codes in the Orange Book, but at the same time we expressed no view as to whether such an action would succeed. *See Andrx Pharms., Inc. v. Biovail Corp.,* 276 F.3d 1368, 1379 (Fed.Cir.2002). To succeed in such an action, the ANDA applicant would ***1382** have to establish that the

FDA's refusal to police use codes was arbitrary and capricious, or contrary to the statute. 5 U.S.C. § 706(2)(A) . We have subsequently held that the FDA is under no statutory obligation to determine the correctness of particular patent listings in the Orange Book, and that nothing in the Hatch-Waxman Act requires the FDA to screen Orange Book submissions by NDA applicants and refuse those that do not satisfy the statutory requirements for listing. *See Apotex,* 347 F.3d at 1349; *see also aaiPharma Inc. v. Thompson,* 296 F.3d 227, 238-40 (4th Cir.2002). Moreover, the very enactment of the counterclaim provision assumed that no alternative remedy was available to an ANDA applicant challenging an Orange Book listing. Today's decision strikingly limits the counterclaim provision with the consequence that, in all likelihood, the ANDA applicant is left without any remedy to correct an erroneous Orange Book listing with respect to a method of use patent. This cannot be what Congress intended.

* * *

In summary, the majority's crabbed view of the statute sanctions an unjustified manipulation of the Orange Book. In this suit, Caraco seeks to compel Novo to correct the use code for PRANDIN, and to reinstate the earlier U-546 use code describing the '358 patent as covering the "USE OF REPAGLINIDE IN COMBINATION WITH METFORMIN TO LOWER BLOOD GLUCOSE." Under the correct construction of the counterclaim provision, the district court properly held that Caraco was entitled to an order reinstating the former U-546 use code. See *Novo Nordisk,* 656 F.Supp.2d 729.

In holding that the counterclaim provision is unavailable, the majority's approach is notably inconsistent with the approach adopted by our sister circuit in another recent Hatch-Waxman Act case, *Teva Pharmaceuticals USA, Inc. v. Sebelius,* 595 F.3d 1303 (D.C.Cir.2010). There the court construed another provision of the 2003 amendments concerning the NDA holder's withdrawal of "patent information submitted under subsection (b) or (c)." 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC). The statute provided that if such information were "withdrawn by the holder of the application," the period of exclusivity of the ANDA first filer would be forfeited. *See id.* The court held that only the withdrawal resulting from a successful counterclaim suit triggered a forfeiture and not a voluntary withdrawal. *Teva*, 595 F.3d at 1317. This was so because there was " *not a single cogent reason* why Congress might have permitted brand manufacturers to trigger subsection (CC) by withdrawing a challenged patent, outside the counterclaim scenario," *id.* (emphasis in original), and because of the strong policy of the statute favoring the 180-day marketing exclusivity period. *Id.* at 1318. Here the majority reaches a result that is unsupported by any cogent reason for leaving an ANDA applicant without a remedy to correct an erroneous Orange Book listing with respect to a method of use patent, and is directly contrary to the congressional purpose. I respectfully dissent.

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615 F.3d 1374, 95 U.S.P.Q.2d 1880
(Cite as: 615 F.3d 1374)

H

United States Court of Appeals,
Federal Circuit.
NOVO NORDISK a/s and Novo Nordisk, Inc.,
Plaintiffs–Appellants,
v.
CARACO PHARMACEUTICAL LABORATORIES, LTD., and Sun Pharmaceutical Industries, Ltd., Defendants–Appellees.

No. 2010–1001.
July 29, 2010.

Appeal from the United States District Court for the Eastern District of Michigan, in case no. 2:05–CV–40188, Judge Avern Cohn.

James F. Hurst, Winston & Strawn LLP, of Chicago, IL, filed a combined petition for panel hearing and rehearing en banc for defendants-appellees. With him on the petition were Charles B. Klein, Steffen N. Johnson, Scott H. Blackman, and Andrew C. Nichols, of Washington, DC; David S. Bloch, of San Francisco, CA.

Josh A. Krevitt, Gibson, Dunn & Crutcher LLP, of New York, NY, filed a response to the petition for plaintiffs-appellants. With him on the response were Mark A. Perry, of Washington, DC; Wayne Barsky, of Los Angeles, CA; and Michael A. Sitzman, of San Francisco, CA.

William A. Rakoczy, Rakoczy Molino Mazzochi Siwik LLP, of Chicago, IL, for amicus curiae Generic Pharmaceutical Association.

Shashank Upadhye, Apotex, Inc., of Toronto, ON Canada, for amicus curiae Apotex, Inc. With him on the brief was Michael A. Berta, Wilson Sonsini Goodrich & Rosati, of San Francisco, CA, for Impax Laboratories, Inc.

David A. Balto, The Law Offices of David A. Balto, of Washington, DC, for amici curiae Consumer Federation of America and National Legislative Association on Prescription Drug Prices.

Shannon M. Bloodworth, Perkins Coie LLP, of Washington, DC, for amicus curiae Mylan Pharmaceuticals Inc.

Michael D. Shumsky, Kirkland & Ellis LLP, of Washington, DC for amicus curiae Teva Pharmaceuticals USA, Inc.

Before RADER, Chief Judge,[FN*] NEWMAN, CLEVENGER,[FN**] LOURIE, BRYSON, GAJARSA, LINN, DYK, PROST, and MOORE, Circuit Judges.

FN* Randall R. Rader assumed the position of Chief Judge on June 1, 2010.

FN** Raymond C. Clevenger, III took part in the decision on the panel rehearing.

GAJARSA, Circuit Judge, with whom DYK, Circuit Judge, joins, dissents from the denial of the petition for rehearing en banc.

ORDER

PER CURIAM.

Defendants–Appellees Caraco Pharmaceutical Laboratories, Ltd. and Sun Pharmaceutical Industries, Ltd. ("Caraco and Sun") filed a combined petition for panel rehearing and rehearing en banc. The panel invited a response from Plaintiffs–Appellants Novo Nordisk A/S and Novo ***1375** Nordisk, Inc. The court granted leave to file briefs amici curiae to Teva Pharmaceuticals, USA, Inc., Mylan Pharmaceuticals Inc., Apotex Inc. and Impax Laboratories, Inc., Consumer Federation of America and National Legislative Association on Prescription Drug Prices, and Generic Pharmaceutical Association.

The petition for rehearing was considered by the panel that heard the appeal, and thereafter the

petition for rehearing en banc, the response to the petition, and briefs amici curiae were referred to the circuit judges who are authorized to request a poll on whether to rehear the appeal en banc. A poll was requested, taken, and failed.

Upon consideration thereof,

IT IS ORDERED THAT:

(1) The petition of Defendants–Appellees Caraco and Sun for panel rehearing is denied.

(2) The petition of Defendants–Appellees Caraco and Sun for rehearing en banc is denied.

(3) The mandate of the court will issue on August 5, 2010.

ON PETITION FOR REHEARING EN BANC

GAJARSA, Circuit Judge, with whom DYK, Circuit Judge, joins, dissenting from the denial of the petition for rehearing en banc.

This case involves the statutory construction of 21 U.S.C. § 355(j)(5)(C)(ii) ("counterclaim provision"), a critical provision of the Hatch–Waxman Act ("HWA") that has not previously been construed.[FN1] In 2003, Congress enacted the counterclaim provision in order to prevent patent holders from making unwarranted or inaccurate claims of patent coverage in the Orange Book.[FN2] Patent holders previously made such claims in order to delay the onset of competition from generic drug manufacturers, by preventing or delaying FDA approval of a generic manufacturer's Abbreviated New Drug Application ("ANDA").[FN3] In *Mylan Pharmaceuticals, Inc. v. Thompson,* 268 F.3d 1323 (Fed.Cir.2001), this court held that generic drug manufacturers could not sue to correct inaccurate and expansive Orange Book listings, thus inspiring Congress to amend the HWA to include the counterclaim provision. The majority's opinion construes the counterclaim provision contrary to its ***1376** manifest Congressional purpose. That construction renders 21 U.S.C. § 355(j)(2)(A)(viii) ("Section viii") carve-out statements a virtual nullity and leaves generic drug manufacturers without a remedy to challenge inaccurate Orange Book listings with respect to method of use patents. Therefore, I respectfully dissent from the court's denial of Caraco's petition for rehearing en banc.

FN1. The counterclaim provision provides:

> (ii) Counterclaim to infringement action
>
> (I) In general
>
> If an owner of the patent or the holder of the approved application under subsection (b) of this section for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) of this section on the ground that the patent does not claim either—
>
> (aa) the drug for which the application was approved; or
>
> (bb) an approved method of using the drug.

FN2. Under the HWA, Congress required the Food and Drug Administration ("FDA") to maintain and publish a list of patents associated with approved drugs and methods of use. *See* 21 U.S.C. § 355(b)(1) (2006). The Orange Book, or the Approved Drug Products with Therapeutic Equivalence Evaluations, implements this statutory mandate. *See* 21 C.F.R. § 314.53(c)(2)(i)(O).

FN3. A generic manufacturer may piggyback on the safety and efficacy data the original drug manufacturer submitted in its "New Drug Application" ("NDA"), and

may seek approval for an identical method of use for its identical generic product by submitting an ANDA. *See* 21 U.S.C. § 355(j).

The background and facts of this case are well laid out in Judge Dyk's dissent in the original panel decision. *See Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.,* 601 F.3d 1359, 1370–78 (Fed.Cir.2010) (Dyk, J., dissenting). As the dissent explains, the majority's opinion adopts an overly narrow construction of "patent information" and an overly broad construction of "an approved method of using the drug." *See id.* at 1370–72, 1376–78. Both constructions are irreconcilable with pre-existing FDA regulations, the text of the HWA, and Congressional intent. *See id.* at 1370–78. I believe rehearing the case en banc is necessary to rectify these improper constructions.

Not only is the majority's construction of the counterclaim provision erroneous, it also eliminates the careful balance Congress has struck between encouraging pharmaceutical discoveries and ensuring that the American people have access to low cost generic drugs. Specifically, the majority's opinion seriously undermines Section viii, a critical provision of the HWA that facilitates the approval and marketing of lower-cost generic drugs for uses no longer protected by a patent.

Under the HWA, Section viii comes into play when a patent listed in the Orange Book "claims one, but not all, approved methods of using a drug." *Id.* at 1365. Section viii permits a generic manufacturer seeking to market an approved use of a drug to certify that its method of using the drug (as described on its label) is not covered by a patent in the Orange Book. Normally, the label associated with the generic version of a drug must be exactly the same as the label associated with the drug approved in the original New Drug Application. 21 U.S.C. § 355(j)(2)(A)(v), (j)(4)(G); 21 C.F.R. § 314.94(a)(8)(iv). A Section viii statement allows a generic manufacturer to avoid infringement by deleting patented used from its proposed label information, thus allowing it to avoid infringement. 21 U.S.C. § 355(j)(2)(A)(viii).

Congress intended Section viii to facilitate the approval and marketing of lower-cost generic drugs, while still respecting the patent rights of pioneering drug manufacturers. Pioneering drug manufacturers, however, have found another way to game the system by subverting Section viii carve-out statements and delaying the onset of generic competition by submitting overbroad and inaccurate use codes. Use codes are codes created by patent holders in Orange Book listings to identify the scope of their Orange Book patents. The FDA will not approve a generic manufacturer's Section viii proposed label amendment if a use code covers the proposed label. Importantly, the FDA makes no effort to determine the accuracy of use codes.[FN4]

FN4. The FDA has maintained, and we have affirmed, that its role in listing patents in the Orange Book is "ministerial"; it simply lists the patent information that it receives from brand manufacturers, expecting those parties to properly abide by the statutory and regulatory mandates. *See Apotex, Inc. v. Thompson,* 347 F.3d 1335, 1349 (Fed.Cir.2003); Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30–Month Stays on Approval of Abbreviated New Drug Applications Certifying that a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 68 Fed.Reg. 36,676, 36,683 (June 18, 2003) (codified at 21 C.F.R. pt. 314).

***1377** In this case, Novo Nordisk (the brand drug manufacturer) owns a patent on the chemical composition of repaglinide, which expired on March 14, 2009. *See* U.S. Patent No. RE 37,035 ("the '035 patent"). Novo also owns a patent on the use of repaglinide in combination with metformin to treat diabetes, which does not expire until 2018. *See* U.S. Patent No. 6,677,358 ("the '358 patent").

In addition to its combination with metformin to treat diabetes, the FDA had approved repaglinide for two other uses: (1) by itself, i.e. monotherapy and (2) in combination with thiazolidinediones. *See Novo Nordisk,* 601 F.3d at 1362. Novo does not own any patents covering the latter two approved uses.

In anticipation of the '035 patent's expiration, Caraco, the generic manufacturer, sought to market the monotherapy use of repaglinide to treat diabetes , a use no longer covered by a patent. In June 2005, Novo sued Caraco, claiming that if Caraco marketed repaglinide, it would nonetheless infringe the '358 patent because Caraco's label would suggest the use of repaglinide together with metformin. Following the FDA's suggestion, Caraco sought a Section viii carve-out statement, making clear that it was not seeking approval to market the use of repaglinide in combination with metformin and limiting its label to the monotherapy use.

To defeat this Section viii carve-out statement, Novo changed the Orange Book use code associated with the '358 patent from "use of repaglinide in combination with metformin to lower blood glucose" to "a method for improving glycemic control in adults with type 2 diabetes mellitus." *See id.* at 1362–63. The latter use code unmistakably covering both patented and unpatented uses. Because the FDA declined to police this inaccurate listing, Caraco asserted the counterclaim provision in the underlying HWA litigation and requested that Novo revise its use code to reflect the '358 patent's true scope.[FN5] The majority opinion, however, held that counterclaim relief is not available because the '358 patent covered at least one approved use. *See id.* at 1364–65. This effectively allows a patent holder to extend its monopoly to unpatented uses.

> FN5. Novo argued, and the majority and concurrence agreed, that this predicament was somehow the fault of the FDA, which had required Novo (and all oral diabetes drug manufacturers) to change the "Indications" part of the drug label for therapeutic reasons. As explained in the dissenting opinion, Novo admits that the FDA did not require Novo's inaccurate listing. *Novo Nordisk,* 601 F.3d at 1380 (Dyk, J. dissenting).

The majority opinion thus eviscerates Section viii. A generic, like Caraco, cannot use Section viii if the pioneering manufacturer's use code is erroneously broad. With the majority's blessing, pioneering drug manufacturers now have every incentive to follow Novo's lead and draft exceedingly broad use codes thereby insulating themselves from generic competition and rendering Section viii a dead letter.

The evisceration of Section viii is exacerbated by the fact that, as Judge Clevenger points out in his concurring opinion in the panel decision, the majority decision likely leaves generic manufacturers such as Caraco with no other remedy. *See Novo Nordisk,* 601 F.3d at 1367–68 (Clevenger, J., concurring). The FDA declined to grant Caraco's Section viii carve-out because the broad use code for the '358 patent now appears to cover Caraco's proposed carve-out label. Caraco also cannot disprove infringement in the infringement lawsuit because the FDA requires it to use Novo's original label, which includes information regarding the patented combination therapy. Thus, Caraco will apparently have to wait to launch its generic repaglinide product***1378** until 2018, the date on which Novo's '358 patent on the combination therapy expires—despite the fact that the '358 patent *concededly does not cover the use for which Caraco seeks to market the drug.* This is an untenable and absurd result, and contravenes the intent of Congress in adopting the counterclaim provision.

Finally, the majority opinion effectively invalidates the FDA's effort to define "patent information" for the purposes of the counterclaim provision. *See Novo Nordisk,* 601 F.3d at 1366–67. This invalidation is especially troubling given Congress's explicit approval of those regulations. *See Legislative and Regulatory Responses to the FTC*

Study on Barriers to Entry in the Pharmaceutical Marketplace: Hearing Before the S. Comm. on the Judiciary, 108th Cong. 19 (2003) (Statement of Sen. Schumer) ("The bill provides a critical complement to the work the FDA has done in clarifying its regulations on patent listing, but it goes much further."). Without even requesting the views of the FDA, the majority opinion refuses to give effect to the FDA's interpretation of an important statutory term. *See Apotex, Inc. v. Thompson,* 347 F.3d 1335, 1351–52 (Fed.Cir.2003) ("Deference is due to an administrative agency's regulations particularly when the subject matter of the regulatory authority is a highly detailed regulatory program to which the agency has brought its specialized expertise, a characterization that aptly describes the FDA's role in the context of the regulatory scheme created pursuant to the Hatch–Waxman Act." (citation and quotations omitted)).

Because the majority's statutory construction of the counterclaim provision abrogates the HWA and frustrates the clear intent of Congress, I dissent from the court's denial of Caraco's request for rehearing en banc.

C.A.Fed. (Mich.),2010.
Novo Nordisk A/S v. Caraco Pharmaceutical Laboratories, Ltd.
615 F.3d 1374, 95 U.S.P.Q.2d 1880

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165 F.3d 1353, 49 U.S.P.Q.2d 1464
(Cite as: 165 F.3d 1353)

United States Court of Appeals,
Federal Circuit.
In Re Joyce A. CORTRIGHT,

No. 98-1258.
Jan. 19, 1999.
Rehearing Denied April 20, 1999.

Applicant who sought patent for method of treating baldness through application of commercially available product used to soften cow udders appealed from decision of the Board of Patent Appeals and Interferences that sustained rejection of two claims. The Court of Appeals, Mayer, Chief Judge, held that: (1) written description was sufficient to support breadth of claim reciting method to "restore hair growth," and (2) second claim, which recited method of offsetting effects of lower levels of male hormone and stated that invention's active agent reached the papilla, did not satisfy patent statute's "how to use" requirement.

Affirmed in part, reversed in part, and remanded.

West Headnotes

[1] Patents 291 314(5)

291 Patents
291XII Infringement
291XII(B) Actions
291k314 Hearing
291k314(5) k. Questions of law or fact. Most Cited Cases

Whether making and using an invention would have required undue experimentation, and thus whether a disclosure is sufficiently enabling under patent statute, is a legal conclusion based upon underlying factual inquiries. 35 U.S.C.A. § 112.

[2] Patents 291 314(5)

291 Patents
291XII Infringement
291XII(B) Actions
291k314 Hearing
291k314(5) k. Questions of law or fact. Most Cited Cases

Patents 291 324.55(2)

291 Patents
291XII Infringement
291XII(B) Actions
291k324 Appeal
291k324.55 Questions of Fact, Verdicts, and Findings
291k324.55(2) k. Clearly erroneous findings. Most Cited Cases

Utility of claimed invention is a factual issue, which Court of Appeals reviews for clear error. 35 U.S.C.A. § 101.

[3] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

A lack of enablement rejection under the patent statute is appropriate where the written description fails to teach those in the art to make and use the invention as broadly as it is claimed without undue experimentation. 35 U.S.C.A. § 112.

[4] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Patent applicant's failure to disclose how to use an invention may support a rejection either for lack of enablement, as a result of the specification's failure to disclose adequately to one ordinarily skilled in the art how to use the invention without undue experimenta-

tion, or for lack of utility when there is a complete absence of data supporting the statements which set forth the desired results of the claimed invention. 35 U.S.C.A. §§ 101, 112.

[5] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Patent and Trademark Office (PTO) cannot make dual rejection of patent application, for both lack of enablement and lack of utility, unless PTO has reason to doubt the objective truth of the statements contained in the written description; PTO may establish a reason to doubt an invention's asserted utility when the written description suggests an inherently unbelievable undertaking or involves implausible scientific principles. 35 U.S.C.A. §§ 101, 112.

[6] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Written description in proposed patent claim for method of treating baldness through application of commercially available product used to soften cow udders was sufficient to support breadth of claim reciting method to “restore hair growth,” despite lack of results showing that user's hair would be returned to its original state, namely, a full head of hair, where term “restore,” as used in prior art, did not mean returning user's hair to its original state, but only that claimed method increased amount of hair grown, and claim's dosing instructions enabled one of ordinary skill to practice claimed invention without need for any experimentation. 35 U.S.C.A. § 112.

[7] Patents 291 101(2)

291 Patents
291IV Applications and Proceedings Thereon
291k101 Claims
291k101(2) k. Construction in general. Most Cited Cases

Although the Patent and Trademark Office (PTO) must give claims their broadest reasonable interpretation, this interpretation must be consistent with the one that those skilled in the art would reach.

[8] Patents 291 161

291 Patents
291IX Construction and Operation of Letters Patent
291IX(A) In General
291k161 k. State of the art. Most Cited Cases

Prior art references may be indicative of what all those skilled in the art generally believe a certain term in a patent means and can often help to demonstrate how a disputed term is used by those skilled in the art.

[9] Patents 291 161

291 Patents
291IX Construction and Operation of Letters Patent
291IX(A) In General
291k161 k. State of the art. Most Cited Cases

Interpretation of claim terms by Patent and Trademark Office (PTO) should not be so broad that it conflicts with the meaning given to identical terms in other patents from analogous art.

[10] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Proposed patent claim for method of treating baldness, which recited method of offsetting effects of lower levels of male hormone and stated that invention's active agent reached the papilla, did not satisfy patent statute's “how to use” requirement, although applicant was not required to prove cause of resultant hair growth as required by Board of Patent Appeals and Interferences, where written description failed to disclose that active ingredient in fact reached the pa-

pilla or that offsetting occurred, nor was it shown that one of ordinary skill would necessarily conclude from information expressly disclosed by written description that active ingredient reached the papilla or that off-setting occurred. 35 U.S.C.A. § 112.

[11] Patents 291 ⚿7.2

291 Patents
291I Subjects of Patents
291k4 Arts
291k7.2 k. Knowledge or appreciation of inventors. Most Cited Cases

It is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works.

[12] Patents 291 ⚿99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases
(Formerly 291k97)

Statements in patent application that a physiological phenomenon was observed are not inherently suspect simply because the underlying basis for the observation cannot be predicted or explained.

Patents 291 ⚿328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original utility. Most Cited Cases

4,139,619, 5,494,667, 5,578,599, 5,597,575, 5,665,342, 5,674,510, 5,679,378, 5,695,748, 5,744,128, 5,750,108, 5,767,152, 5,777,134, 5,800,477. Cited as prior art.

***1354** Joseph B. Taphorn, of Poughkeepsie, New York, argued for appellant.

Scott A. Chambers, Associate Solicitor, U.S. Patent and Trademark Office, of Arlington, Virginia, argued for the appellee. With him on the brief were Nancy J. Linck, Solicitor, Albin F. Drost, Deputy Solicitor, and Linda Moncys Isacson, Associate Solicitor.

Before MAYER, Chief Judge, NEWMAN, and RADER, Circuit Judges.

***1355** MAYER, Chief Judge.

Joyce A. Cortright appeals the September 23 and November 28, 1997, decisions of the United States Board of Patent Appeals and Interferences sustaining the rejection of claims 1 and 15 of patent application Serial No. 07/849,191 under 35 U.S.C. § 112, ¶ 1 (1994). Because the board erred with respect to claim 1 but not claim 15, we affirm-in-part, reverse-in-part, and remand.

Background

Cortright's patent application, filed in 1992, concerns a method of treating baldness by applying Bag Balm®, a commercially available product used to soften cow udders, to human scalp. Claims 1 and 15 are the only claims on appeal. Claim 1 recites a method of "treating scalp baldness with an antimicrobial to restore hair growth, which comprises rubbing into the scalp the ointment wherein the active ingredient 8-hydroxy-quinoline sulfate 0.3% is carried in a petrolatum and lanolin base." Claim 15 recites a method of "offsetting the effects of lower levels of a male hormone being supplied by arteries to the papilla of scalp hair follicles with the active agent 8-hydroxy-quinoline sulfate to cause hair to grow again on the scalp, comprising rubbing into the scalp the ointment having the active agent 8-hydroxy-quinoline sulfate 0.3% carried in a petrolatum and lanolin base so that the active agent reaches the papilla."

The examiner rejected the claims under 35 U.S.C. § 101 (1994) as lacking utility. According to the examiner, Cortright's statements of utility, namely, her claims of treating baldness, are suspect because "baldness is generally accepted in the art as being incurable...." The examiner, therefore, required clinical evidence to establish the claimed utility, which Cortright did not supply. Furthermore, with respect to claim 15's recitation of offsetting the effects of lower levels of a male hormone, Cortright "offered no proof that such an off-set occurs and has disclosed that this is only speculation." The examiner also rejected the

claims under 35 U.S.C. § 102(a) (1994), arguing that the admitted prior art anticipates the claims because the written description discloses that Bag Balm® has been applied to human skin and the "scalp is the skin of the head." Cortright appealed these rejections to the Board of Patent Appeals and Interferences.

In its September 23, 1997, decision, the board reversed the section 101 rejection because the examiner did not set out sufficient reasons for finding Cortright's statements of utility incredible. It noted that "there is no per se requirement for clinical evidence to establish the utility of any invention" and the examples in Cortright's application are objective evidence. The board also reversed the section 102(a) rejection because although the prior art discloses the application of Bag Balm® to human skin, it does not disclose applying it to bald, human scalp.

Despite these reversals, Cortright did not prevail because the board found a new ground for rejecting the claims: that they are based on a non-enabling disclosure in violation of 35 U.S.C. § 112, ¶ 1. The board found that Cortright's written description does not teach those of ordinary skill in the art how to make and use the claimed invention without undue experimentation because it "fails to provide any teachings as to the administration of Bag Balm® in a manner which (i) restore[s] hair growth (claim 1), or (ii) 'offset [s] the effects of lower levels of male hormone being supplied by arteries to the papilla of scalp hair follicles' (claim 15)." The board explained that Example 1 does not show that applying a teaspoon of Bag Balm® to the scalp daily for about one month "restored hair growth" and that Examples 2 and 3 do not disclose the amount of Bag Balm® to apply or how to restore hair growth. With respect to claim 15, the board found that the written description "merely surmis[es] that the active ingredient, 8-hydroxy-quinoline sulfate, even reaches the papilla," which would not enable one of ordinary skill to use the claimed method. Finally, the board observed that the breadth of the claims and the unpredictable nature of the art of hair growth aggravated its finding that those of ordinary skill in the art would not be able to practice the invention without undue experimentation.

Cortright requested reconsideration, which the board denied in a November 28, 1997, ***1356** opinion. The board explained that claim 1 is not enabled because it claims "restor[ing] hair growth," which the board interpreted as requiring the user's hair "to return to its original state," that is, a full head of hair. Thus, the board's rejection was not based on complete non-enablement, as the original decision had implied, but on the claim not being commensurate with the scope of the disclosure. With respect to claim 15, the board maintained its general non-enablement rejection, adding that "there is no evidence of record that the resultant hair growth is due to (i) the stimulation of the papilla, and (ii) the offsetting [of] the effects of lower male hormone which is supplied by arteries to the papilla, and not due to some other mechanism(s)." Cortright appeals.

Discussion

[1][2] "Whether making and using an invention would have required undue experimentation, and thus whether a disclosure is enabling under 35 U.S.C. § 112, ¶ 1 (1994), is a legal conclusion based upon underlying factual inquiries." *Johns Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1354, 47 USPQ2d 1705, 1713 (Fed.Cir.1998). Utility is a factual issue, which we review for clear error. *See Cross v. Iizuka*, 753 F.2d 1040, 1044 n. 7, 224 USPQ 739, 742 n. 7 (Fed.Cir.1985); *see also In re Zurko*, 142 F.3d 1447, 1449, 46 USPQ2d 1691, 1693 (Fed.Cir.), *cert. granted*, 525 U.S. 961, 119 S.Ct. 401, 142 L.Ed.2d 326 (1998).

[3] Section 112, ¶ 1 provides:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 112, ¶ 1. A lack of enablement rejection under section 112, ¶ 1 is appropriate where the written description fails to teach those in the art to make and use the invention as broadly as it is claimed without undue experimentation. *See In re Vaeck*, 947 F.2d 488, 495-96, 10 USPQ2d 1438, 1444 (Fed.Cir.1991).

This rejection takes several forms. The PTO will make a scope of enablement rejection where the written description enables something within the

scope of the claims, but the claims are not limited to that scope. *See* Manual of Patent Examining Procedures ("M.P.E.P.") § 706.03(c), form ¶ 7.31.03 (Rev.3, July 1997). This type of rejection is marked by language stating that the specification does not enable one of ordinary skill to use the invention commensurate with the scope of the claims. On the other hand, if the written description does not enable any subject matter within the scope of the claims, the PTO will make a general enablement rejection, stating that the specification does not teach how to make or use the invention. *See* M.P.E.P. § 706.03(c), form ¶ 7.31.02.

[4] If the written description fails to illuminate a credible utility, the PTO will make both a section 112, ¶ 1 rejection for failure to teach how to use the invention and a section 101 rejection for lack of utility. *See* M.P.E.P. § 706.03(a), form ¶ 7.05.04. This dual rejection occurs because "[t]he how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention." *In re Ziegler*, 992 F.2d 1197, 1200, 26 USPQ2d 1600, 1603 (Fed.Cir.1993). Thus, an applicant's failure to disclose how to use an invention may support a rejection under either section 112, ¶ 1 for lack of enablement as a result of "the specification's ... failure to disclose adequately to one ordinarily skilled in the art 'how to use' the invention without undue experimentation," or section 101 for lack of utility "when there is a complete absence of data supporting the statements which set forth the desired results of the claimed invention." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed.Cir.1984); *see also In re Brana*, 51 F.3d 1560, 1564 n. 12, 34 USPQ2d 1436, 1439 n. 12 (Fed.Cir.1995) (The "absence of utility can be the basis of a rejection under both 35 U.S.C. § 101 and § 112 ¶ 1."); *In re Fouche*, 58 C.C.P.A. 1086, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971) ("[I]f ***1357** [certain] compositions are in fact useless, appellant's specification cannot have taught how to use them.").

[5] The PTO cannot make this type of rejection, however, unless it has reason to doubt the objective truth of the statements contained in the written description. *See Brana*, 51 F.3d at 1566, 34 USPQ2d at 1441 ("[T]he PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.") (citations omitted); *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) ("[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."). The PTO may establish a reason to doubt an invention's asserted utility when the written description "suggest[s] an inherently unbelievable undertaking or involve[s] implausible scientific principles." *Brana*, 51 F.3d at 1566, 34 USPQ2d at 1441; *see also In re Eltgroth*, 57 C.C.P.A. 833, 419 F.2d 918, 164 USPQ 221 (CCPA 1970) (control of aging process). Treating baldness was once considered an inherently unbelievable undertaking. *See In re Ferens*, 57 C.C.P.A. 733, 417 F.2d 1072, 1074, 163 USPQ 609, 611 (CCPA 1969); *In re Oberweger*, 28 C.C.P.A. 749, 115 F.2d 826, 829, 47 USPQ 455, 458 (CCPA 1940).

Since then, however, treatments for baldness have gained acceptance. Rogaine® (minoxidil) and Propecia® are recognized as effective in treating baldness. *See* Doug Levy, *FDA Approves New Treatment for Males Fighting Baldness*, USA Today, Dec. 23, 1997, at A1; *Pharmaceutical Companies Are Brushing up on Hair-Restorers Medicine*, Los Angeles Times, Jun. 6, 1996, at D12. In addition, the PTO has granted approximately one hundred patents on methods of treating baldness. Some of these patents disclose applying an electric current to the scalp, *see, e.g.*, U.S. Pat. No. 5,800,477, whereas others teach ingesting substances orally or applying a salve of some kind to the scalp, *see, e.g.*, U.S. Pat. No. 5,777,134. Some patents disclose the active ingredient in chemical terms. *See, e.g.*, U.S. Pat. No. 5,777,134 (5 alpha-reductase inhibitor); U.S. Pat. No. 5,767,152 (cyanocarboxylic acid derivatives); U.S. Pat. No. 4,139,619 (formula for minoxidil). Other patents, however, disclose baldness remedies made from more mundane materials, such as Dead Sea mud (U.S.Pat. No. 5,679,378); emu oil (U.S.Pat. No. 5,744,128); potato peelings and lantana leaves (U.S.Pat. No. 5,665,342); and vitamin D3 and aloe (U.S.Pat. No.

5,597,575).[FN*]

FN* *See also* U.S. Pat. No. 5,674,510 (salve of garlic powder, brewer's yeast, grapefruit juice, acetic acid, and kelp), U.S. Pat. No. 5,750,108 (salves of tea tree oil; chlorine dioxide and acidic solution; saw palmetto berry extract), U.S. Pat. No. 5,695,748 (salves of sage, aloe, and nettles; castor oil, shea butter, wheat germ oil, and white iodine); U.S. Pat. No. 5,494,667 (salve of pine extract and bamboo extract or Japanese apricot).

Claim 1

[6] With respect to claim 1, the examiner made a lack of utility rejection under section 101 arguing that the asserted statements of utility were incredible in light of Cortright's failure to prove utility with clinical evidence. The board first appeared to make a generic enablement rejection under section 112, ¶ 1, focusing on "the lack of any teachings or guidance as to how to perform the claimed methods and the unpredictable nature of the art of restoring hair growth." Upon reconsideration, however, the board clarified that its rejection pertained to scope. It took the position that the broadest interpretation of "restore hair growth" requires the application of Bag Balm® to "return" the user's hair "to its original state," that is, a full head of hair. Because Cortright's written description discloses results of only "three times as ***1358** much hair growth as two months earlier," "filling-in some," and "fuzz," the board reasoned, it does not support the breadth of the claims.

[7][8][9] Although the PTO must give claims their broadest reasonable interpretation, this interpretation must be consistent with the one that those skilled in the art would reach. *See In re Morris*, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed.Cir.1997) ("[T]he PTO applies to the verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art...."); *In re Bond*, 910 F.2d 831, 833, 15 USPQ2d 1566, 1567 (Fed.Cir.1990) ("It is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification, ... and that claim language should be read in light of the specification *as it would be interpreted by one of ordinary skill in the art.* ") (emphasis added); *see also* M.P.E.P. § 2111.01 ("[T]he words of a claim ... must be read as they would be interpreted by those of ordinary skill in the art."). Prior art references may be "indicative of what all those skilled in the art generally believe a certain term means ... [and] can often help to demonstrate how a disputed term is used by those skilled in the art." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584, 39 USPQ2d 1573, 1578-79 (Fed.Cir.1996). Accordingly, the PTO's interpretation of claim terms should not be so broad that it conflicts with the meaning given to identical terms in other patents from analogous art. *Cf. Morris*, 127 F.3d at 1056, 44 USPQ2d at 1029 (approving the board's definition of claim terms consistent with their definitions in CCPA cases).

The PTO's construction of "restore hair growth" in the present case is inconsistent with its previous definitions. U.S. Pat. Nos. 5,695,748 ("the '748 patent"), 5,679,378 ("the '378 patent"), and 5,578,599 ("the '599 patent"), for example, each recite a method of restoring hair growth. The '748 patent recites:

> A process ... for *restoring hair growth* which comprises the steps of:
>
> (a) applying a cleansing mixture of sage, aloe and nettles to the hair and scalp in an amount and for a period of time sufficient to effect cleansing and then removing same;
>
> (b) applying a treatment mixture of castor oil, shea butter, wheat germ oil and white iodine to the hair and scalp in an amount and for a period of time effective to treat the hair and scalp; and
>
> (c) heating the treatment mixture on the hair and scalp for a period of time sufficient to promote penetration of the treatment mixture into the hair and scalp and then removing the treatment mixture.

'748 patent (Claim 1) (emphasis added). The accompanying disclosure reveals five examples in which women and men practiced the claimed method. One "subject's hair began to fill-in in the previously balding and thinning areas and the subject ... achieved a significant degree of improvement...." *Id.* (Example 3). For another subject, "there [was] a partial filling-in and restoration of the bald spot on the top of the sub-

ject's head." *Id.* (Example 4). A third subject noticed that he had "fifty percent more hair in both the frontal and middle sections of his scalp." *Id.* (Example 6).

The '378 patent recites:

> The method for *the restoration of hair growth* ... which comprises the steps of:
>
> applying a finite layer of Dead Sea mud to the body surface area to be treated for the restoration of hair growth ...;
>
> allowing said layer to be undisturbed for a finite time; and
>
> rinsing said layer from said surface area.

'378 patent (Claim 1) (emphasis added). The accompanying disclosure reveals an example in which a man noticed "[m]any sprouts of ... new hair" after practicing the method for six weeks and ultimately "approximately 25% regrowth over the entire previously bald scalp." *Id.* (Example 1). Another example discloses the results of a five-month study of men who practiced the invention. In this study, the participants noticed an increase in the number of new hairs on their scalp per month, which varied from 0 to 22. Although ***1359** some participants reported significant growth of hair, there was no evidence that the claimed method resulted in full heads of hair. *See id.* (Example 3).

The '599 patent recites:

> A method for increasing or *restoring hair growth* over the sole administration of a topical minoxidil treatment comprising the concomitant administration of:
>
> a topical preparation of minoxidil in an amount sufficient to promote hair growth, applied to an area of skin where hair growth is to be increased or restored; and
>
> an oral administration of 17 beta-(N-tert-butylcarbamoyl)-4-aza-5-alpha-androst-1-en-3-one in an amount from about 0.05 to about 0.03 mg/Kg to promote hair growth such that hair growth is increased over the administration of minoxidil alone.

'599 patent (Claim 1) (emphasis added). The examples disclosed by the patent show that subjects practicing this method experienced increased growth of hair compared to those using minoxidil alone. Nevertheless, the patent does not show that this method completely cured baldness by producing a full head of hair.

In light of these disclosures, one of ordinary skill would not construe "restoring hair growth" to mean "returning the user's hair to its original state," as the board required. To the contrary, consistent with Cortright's disclosure and that of other references, one of ordinary skill would construe this phrase as meaning that the claimed method increases the amount of hair grown on the scalp but does not necessarily produce a full head of hair. Properly construed, claim 1 is amply supported by the written description because Example 1 discloses the amount of Bag Balm® to apply (about one teaspoon daily) and the amount of time (about one month) in which to expect results. These dosing instructions enable one of ordinary skill to practice the claimed invention without the need for any experimentation. Therefore, we reverse the board's rejection of claim 1.

Claim 15

[10] With respect to claim 15, the examiner made a lack of utility rejection under section 101 because Cortright "offered no proof that such an off-set occurs and has disclosed that this is only speculation." Although the board purported to reject the examiner's section 101 rejection of claim 15, its new rejection under section 112, ¶ 1 suggests that it did not disagree with the examiner entirely. The board stated that because the written description "merely 'surmises' " that the active ingredient, 8-hydroxy-quinoline sulfate reaches the papilla and offsets the lower levels of male hormone, it did not teach how to use the method of claim 15. It observed further that the written description fails to provide a working example of the subject matter of claim 15 or any evidence that "the effects of lower male hormone levels have been offset [by the claimed method], or even if Bag Balm®) has reached the papilla." The board also faulted Cortright for not producing evidence that "the resultant hair growth is due to (i) the stimulation of the papilla, and (ii) the offsetting [of] the effects of lower male hormone which is supplied by arteries to the papilla, and not due to some other mechanism(s)." Moreover, it found that

the written description indicates that "the underlying basis for the observed physiological phenomenon can not [sic] be predicted from the results obtained," and that this type of unpredictability alone may "provide a reasonable doubt as to the accuracy of broad statements made in support of the enablement of a claim."

[11][12] "[I]t is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." *Newman v. Quigg*, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed.Cir.1989); *see also Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed.Cir.1983) ("[I]t is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests."). Furthermore, statements that a physiological phenomenon was observed are not inherently suspect simply because the underlying basis for the observation cannot be predicted or explained. Therefore, the board erred in suggesting that Cortright was required to prove the cause of the resultant hair growth.

***1360** Statements relating to observations that salves applied to the scalp penetrate the skin and reach the papilla or that chemicals affect hormones do not run counter to generally accepted scientific norms. Therefore, a disclosure that the active agent, 8-hydroxy-quinoline sulfate, reached the papilla and offset lower levels of male hormones is not inherently suspect. Nevertheless, we must affirm the rejection of claim 15 because the written description fails to disclose that the active ingredient reaches the papilla or that offsetting occurs. *See In re Bundy*, 642 F.2d 430, 434, 209 USPQ 48, 51 (CCPA 1981) ("What is necessary to satisfy the how-to-use requirement of § 112 is the disclosure of some activity coupled with knowledge as to the use of this activity."). Here, although the written description states that people observed hair growth after applying Bag Balm® to the scalp, it does not disclose that anyone observed the active ingredient reach the papilla and offset the effects of lower levels of male hormones. It states, rather, that "*[i]t is believed* that the rubbed-in ointment offsets the effects of lower levels of male hormones in the papilla and/or provides an antimicrobial effect on infection," and that "Applicant *surmises* that the active antimicrobial agent, 8-hydro[x]y-quinoline sulfate, reaches the papilla, and is effective to off-set the male hormones such as testosterone and/or androsterone, and/or kill or seriously weaken any bacteria about or in the papilla ...." (emphasis added). These statements reflect no actual observations. Moreover, we have not been shown that one of ordinary skill would necessarily conclude from the information expressly disclosed by the written description that the active ingredient reaches the papilla or that off-setting occurs. *See Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1159, 47 USPQ2d 1829, 1834 (Fed.Cir.1998) ("In order for a disclosure to be inherent ... the missing descriptive matter must necessarily be present in the ... application's specification such that one skilled in the art would recognize such a disclosure."); *see also In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981) ("Inherency ... 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.") (quoting *Hansgirg v. Kemmer*, 26 C.C.P.A. 937, 102 F.2d 212, 214, 40 USPQ 665, 667 (CCPA 1939)). Therefore, claim 15 does not satisfy the how to use requirement of section 112, ¶ 1.

Conclusion

Accordingly, the decision of the United States Board of Patent Appeals and Interferences is affirmed in part and reversed in part, and the case is remanded for further proceedings in accordance with this opinion.

COSTS

Each party shall bear its own costs.

AFFIRMED-IN-PART, REVERSED-IN-PART, AND REMANDED

C.A.Fed.,1999.
In re Cortright
165 F.3d 1353, 49 U.S.P.Q.2d 1464

END OF DOCUMENT

51 F.3d 1560, 63 USLW 2656, 34 U.S.P.Q.2d 1436
(Cite as: 51 F.3d 1560)

United States Court of Appeals,
Federal Circuit.
In re Miguel F. BRANA, Jose M.C. Berlanga, Marina M. Moset, Erich Schlick and Gerhard Keilhauer.

93-1393.
March 30, 1995.

Applicants appealed from decision of the United States Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences, affirming patent examiner's rejections of claims for antitumor compound. The Court of Appeals, Plager, Circuit Judge, held that: (1) claimed specification for antitumor compound satisfied statutory utility requirement by alleging that compound was more effective in treating lymphocytic leukemia in mice than other known compounds; (2) PTO failed to satisfy its initial burden of challenging presumptively correct assertion of utility; (3) even if one skilled in the art would have reasonably questioned asserted utility of claimed antitumor compound, applicants provided sufficient evidence to convince one of skill in the art of asserted utility; and (4) Food and Drug Administration (FDA) approval is not prerequisite for finding compound useful within meaning of patent laws.

Reversed.

West Headnotes

[1] Patents 291 101(5)

291 Patents
291IV Applications and Proceedings Thereon
291k101 Claims
291k101(5) k. Requisites and sufficiency. Most Cited Cases

Claim specifications for antitumor compound satisfied statutory utility requirement by alleging that compound was more effective in treating lymphocytic leukemia in mice than other known compounds. 35 U.S.C.A. § 101.

[2] Patents 291 48

291 Patents
291II Patentability
291II(C) Utility
291k48 k. Nature of product or result. Most Cited Cases

Lymphocytic leukemia tumor models used to study cancer in mice represented specific diseases against which claimed compounds in patent application could be effective, as required to satisfy statutory utility requirement, where cell lines used on models were originally derived from lymphocytic leukemias in mice and would produce that disease once implanted in mice. 35 U.S.C.A. § 101.

[3] Patents 291 49

291 Patents
291II Patentability
291II(C) Utility
291k49 k. Evidence of utility. Most Cited Cases
(Formerly 291k97)

Patent and Trademark Office (PTO) has initial burden of challenging presumptively correct assertion of utility in patent disclosure. 35 U.S.C.A. § 101.

[4] Patents 291 49

291 Patents
291II Patentability
291II(C) Utility
291k49 k. Evidence of utility. Most Cited Cases
(Formerly 291k97)

Only after Patent and Trademark Office (PTO) provides evidence showing that one of ordinary skill in art would reasonably doubt asserted utility of patented invention does burden shift to applicant to provide rebuttal evidence sufficient to convince such person of invention's asserted utility. 35 U.S.C.A. §

101.

[5] Patents 291 49

291 Patents
291II Patentability
291II(C) Utility
291k49 k. Evidence of utility. Most Cited Cases
(Formerly 291k97)

Patent and Trademark Office (PTO) failed to satisfy its initial burden of challenging presumptively correct assertion of utility in application for patent for antitumor compound, where references cited by PTO did not question usefulness of any compound as antitumor agent or provide any other evidence to cause one of skill in the art to question asserted utility of applicants' compounds, but instead discussed therapeutic predictive value of tests used in mice, which were relevant only if applicants were required to prove ultimate value in humans of their asserted utility. 35 U.S.C.A. § 101.

[6] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Even if one skilled in the art would have reasonably questioned asserted utility of claimed antitumor compound, applicants provided sufficient evidence to convince one of skill in the art of asserted utility; applicants provided test results showing that several compounds within scope of claims exhibited significant antitumor activity, and prior art disclosed structurally similar compounds which were proven to be effective antitumor agents. 35 U.S.C.A. § 101.

[7] Patents 291 49

291 Patents
291II Patentability
291II(C) Utility
291k49 k. Evidence of utility. Most Cited Cases

Although minor changes in chemical compounds can radically change their effects on human body, evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe asserted utility.

[8] Patents 291 46

291 Patents
291II Patentability
291II(C) Utility
291k46 k. Nature and necessity of patentable utility. Most Cited Cases

Food and Drug Administration (FDA) approval is not prerequisite for finding compound useful within meaning of patent laws. Federal Food, Drug, and Cosmetic Act, § 505(i)(1), 21 U.S.C.A. § 355(i)(1); 35 U.S.C.A. §§ 101, 112; 21 C.F.R. §§ 312.21(b), 312.23(a)(5), (a)(8).

[9] Patents 291 324.5

291 Patents
291XII Infringement
291XII(B) Actions
291k324 Appeal
291k324.5 k. Scope and extent of review in general. Most Cited Cases

In reviewing decisions of Patent and Trademark Office (PTO), Court of Appeals traditionally reviews questions of law without deference to views of the agency, and defers to agency with regard to questions of fact unless its findings are clearly erroneous.

[10] Patents 291 324.55(1)

291 Patents
291XII Infringement
291XII(B) Actions
291k324 Appeal
291k324.55 Questions of Fact, Verdicts, and Findings
291k324.55(1) k. In general. Most Cited Cases

When mixed questions of law and fact are before Court of Appeals on appeal from decision of Patent and Trademark Office (PTO), whether Court of Appeals defers, and extent to which it defers to agency's

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(Cite as: 51 F.3d 1560)

decision, turns on nature of case and nature of judgment. 5 U.S.C.A. § 706.

***1562** Malcolm J. MacDonald, Keil & Weinkauf, Washington, DC, argued, for appellant. With him on the brief was Herbert B. Keil. Of counsel was David S. Nagy.

Fred E. McKelvey, Sol., Office of Sol., Arlington, VA, argued, for appellee. With him on the brief were Albin F. Drost, Deputy Sol., Richard E. Schafer, Teddy S. Gron, Joseph G. Piccolo and Richard L. Torczon, Associate Sols.

Before PLAGER, LOURIE, and RADER, Circuit Judges.

PLAGER, Circuit Judge.

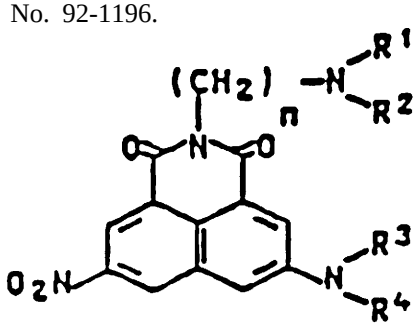
Miguel F. Brana, *et al.* (applicants), appeal the March 19, 1993 decision of the United States Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences (Board), in Appeal No. 92-1196. The Board affirmed the examiner's rejection of claims 10-13 of patent application Serial No. 533,944 under 35 U.S.C. § 112 ¶ 1 (1988).[FN1] The examiner's rejection, upon which the Board relied in rendering its decision, was based specifically on a challenge to the utility of the claimed compounds and the amount of experimentation necessary to use the compounds. We conclude the Board erred, and reverse.

FN1. Unless otherwise noted, all United States Code citations are to the 1988 edition.

I. BACKGROUND

On June 30, 1988, applicants filed patent application Serial No. 213,690 (the '690 application) [FN2] directed to 5-nitrobenzo[de]isoquinoline-1,3-dione compounds, for use as antitumor substances, having the following formula:

FN2. This is a divisional of patent application Serial No. 110,871 filed October 21, 1987.



where n is 1 or 2, R^1 and R^2 are identical or different and are each hydrogen, C_1-C_6-alkyl, C_1-C_6-hydroxyalkyl, pyrrolidinyl, morpholino, piperidinyl or piperacinyl, and R^3 and R^4 are identical or different and are each hydrogen, C_1-C_6-alkyl, C_1-C_6-acyl, C_2-C_7-alkoxycarbonyl, ureyl, aminocarbonyl or C_2-C_7-alkylaminocarbonyl. These claimed compounds differ from several prior art benzo[de]isoquinoline-1,3-dione compounds due to the presence of a nitro group (O_2N) at the 5-position and an amino or other amino group (NR^3R^4) at the 8-position of the isoquinoline ring.

The specification states that these non-symmetrical substitutions at the 5-and 8-positions produce compounds with "a better action and a better action spectrum as antitumor substances" than known benzo[de]isoquinolines, namely those in K.D. Paull et al., *Computer Assisted Structure-Activity Correlations*, Drug Research, 34(II), 1243-46 (1984) (Paull). Paull describes a computer-assisted evaluation of benzo[de]isoquinoline-1,3-diones and related compounds which have been screened for antitumor activity by testing their efficacy ***in vivo*** [FN3] against two specific implanted murine (i.e., utilizing mice as test subjects) lymphocytic leukemias, P388 and L1210.[FN4] These two ***in vivo*** tests are ***1563** widely used by the National Cancer Institute (NCI) to measure the antitumor properties of a compound. Paull noted that one compound in particular, benzo[de]isoquinoline-1,3(2H)dione,5-amino-2(2-di methyl-aminoethyl [sic]) (hereinafter "NSC 308847"), was found to show excellent activity against these two specific tumor models. Based on their analysis, compound NSC 308847 was selected for further studies by NCI. In addition to comparing the effectiveness of the claimed compounds with structurally

similar compounds in Paull, applicants' patent specification illustrates the cytotoxicity of the claimed compounds against human tumor cells, ***in vitro,*** [FN5] and concludes that these tests "had a good action." [FN6]

FN3. ***In vivo*** means "[i]n the living body, referring to a process occurring therein." Steadman's Medical Dictionary 798 (25th ed. 1990). ***In vitro*** means "[i]n an artificial environment, referring to a process or reaction occurring therein, as in a test tube or culture media." *Id.*

FN4. The analysis in Paull consisted of grouping the previously-tested compounds into groups based on common structural features and cross-referencing the various groups, in light of the success rates of the group as a whole, to determine specific compounds that may be effective in treating tumors.

FN5. *See supra* note 3.

FN6. The specification does not state the specific type of human tumor cells used in this test.

The examiner initially rejected applicants' claims in the '690 application as obvious under 35 U.S.C. § 103 in light of U.S. Patent No. 4,614,820, issued to and referred to hereafter as Zee-Cheng et al. Zee-Cheng et al. discloses a benzo[de]isoquinoline compound for use as an antitumor agent with symmetrical substitutions on the 5-position and 8-position of the quinoline ring; in both positions the substitution was either an amino or nitro group. [FN7] Although not identical to the applicants' claimed compounds, the examiner noted the similar substitution pattern (i.e., at the same positions on the isoquinoline ring) and concluded that a mixed substitution of the invention therefore would have been obvious in view of Zee-Cheng et al.

FN7. The chemical compound in Zee-Cheng et al. is labeled a 3,6-disubstituted-1,8-naphthalimide and uses different numbering for the positions on the isoquinoline ring. The structure of this compound, however, is identical to that claimed by the applicants except for symmetrical substitutions at the 5-position and the 8-position of the isoquinoline ring. Zee-Cheng et al. teaches identical substitutions of amino or nitro groups while applicants claim a nitro group substitution at the 5-position and an amino group substitution at the 8-position.

In a response dated July 14, 1989, the applicants rebutted the § 103 rejection. Applicants asserted that their mixed disubstituted compounds had unexpectedly better antitumor properties than the symmetrically substituted compounds in Zee-Cheng et al. In support of this assertion applicants attached the declaration of Dr. Gerhard Keilhauer. In his declaration Dr. Keilhauer reported that his tests indicated that applicants' claimed compounds were far more effective as antitumor agents than the compounds disclosed in Zee-Cheng et al. when tested, ***in vitro,*** against two specific types of human tumor cells, HEp and HCT-29.[FN8] Applicants further noted that, although the differences between the compounds in Zee-Cheng et al. and applicants' claimed compounds were slight, there was no suggestion in the art that these improved results (over Zee-Cheng et al.) would have been expected. Although the applicants overcame the § 103 rejection, the examiner nevertheless issued a final rejection, on different grounds, on September 5, 1989.

FN8. HEp cells are derived from laryngeal cancer and HCT-29 cells from colon cancer.

On June 4, 1990, applicants filed a continuation application, Serial No. 533,944 (the '944 application), from the above-mentioned '690 application. Claims 10-13, the only claims remaining in the continuation application, were rejected in a final office action dated May 1, 1991. Applicants appealed the examiner's final rejection to the Board.

In his answer to the applicants' appeal brief, the examiner stated that the final rejection was based on 35 U.S.C. § 112 ¶ 1.[FN9] The examiner first noted that the specification failed to describe any specific disease against which the claimed compounds were active. Furthermore, the examiner concluded that the prior art tests performed in Paull and the tests disclosed in the specification were not sufficient to establish a reasonable expectation that the claimed compounds had ***1564** a practical utility (i.e. antitumor activity in humans).[FN10]

FN9. The examiner's answer noted that the final rejection also could have been made under 35 U.S.C. § 101 for failure to disclose a practical utility.

FN10. The examiner subsequently filed two supplemental answers in response to arguments raised by the applicants in supplemental reply briefs.

In a decision dated March 19, 1993, the Board affirmed the examiner's final rejection. The three-page opinion, which lacked any additional analysis, relied entirely on the examiner's reasoning. Although noting that it also would have been proper for the examiner to reject the claims under 35 U.S.C. § 101, the Board affirmed solely on the basis of the Examiner's § 112 ¶ 1 rejection. This appeal followed.

II. DISCUSSION

At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant prove regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.[FN11] We note the Commissioner has recently addressed this question in his Examiner Guidelines for Biotech Applications, *see* 60 Fed.Reg. 97 (1995); 49 Pat.Trademark & Copyright J. (BNA) No. 1210, at 234 (Jan. 5, 1995).

FN11. *See, e.g., Cross v. Iizuka,* 753 F.2d 1040, 224 USPQ 739 (Fed.Cir.1985); *In re Langer*, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974); *In re Krimmel*, 292 F.2d 948, 130 USPQ 215 (CCPA 1961); *In re Bergel*, 292 F.2d 958, 130 USPQ 205 (CCPA 1961).

The requirement that an invention have utility is found in 35 U.S.C. § 101: "Whoever invents ... any new and *useful* ... composition of matter ... may obtain a patent therefor...." (emphasis added). It is also implicit in § 112 ¶ 1, which reads:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Obviously, if a claimed invention does not have utility, the specification cannot enable one to use it.

As noted, although the examiner and the Board both mentioned § 101, and the rejection appears to be based on the issue of whether the compounds had a practical utility, a § 101 issue, the rejection according to the Board stands on the requirements of § 112 ¶ 1. It is to that provision that we address ourselves.[FN12] The Board gives two reasons for the rejection; [FN13] we will consider these in turn.

FN12. This court's predecessor has determined that absence of utility can be the basis of a rejection under both 35 U.S.C. § 101 and § 112 ¶ 1. *In re Jolles*, 628 F.2d 1322, 1326 n. 11, 206 USPQ 885, 889 n. 11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971) ("[I]f such compositions are in fact useless, appellant's specification cannot have taught how to use them."). Since the Board affirmed the examiner's rejection based solely on § 112 ¶ 1, however, our review is limited only to whether the application complies with § 112 ¶ 1.

FN13. The Board's decision did not expressly make any independent factual determinations or legal conclusions. Rather, the Board stated that it "agree[d] with the examiner's well reasoned, well stated and fully supported by citation of relevant precedent position in every particular, and any further comment which we might add would be redundant." *Ex parte Brana et al.*, No. 92-1196 (Bd.Pat.App. & Int. March 19, 1993) at 2-3. Therefore, reference in this opinion to Board findings are actually arguments made by the examiner which have been expressly adopted by the Board.

1.

[1] The first basis for the Board's decision was

that the applicants' specification failed to disclose a specific disease against which the claimed compounds are useful, and therefore, absent undue experimentation, one of ordinary skill in the art was precluded from using the invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed.Cir.1986), *cert. denied*, 480 U.S. 947, 107 S.Ct. 1606, 94 L.Ed.2d 792 (1987). In support, the Commissioner argues that the disclosed uses in ***1565** the '944 application, namely the "treatment of diseases" and "antitumor substances," are similar to the nebulous disclosure found insufficient in *In re Kirk*, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). This argument is not without merit.

In *Kirk* applicants claimed a new class of steroid compounds. One of the alleged utilities disclosed in the specification was that these compounds possessed "high biological activity." *Id.* at 938, 153 USPQ at 50. The specification, however, failed to disclose which biological properties made the compounds useful. Moreover, the court found that known specific uses of similar compounds did not cure this defect since there was no disclosure in the specification that the properties of the claimed compounds were the same as those of the known similar compounds. *Id.* at 942, 153 USPQ at 53. Furthermore, it was not alleged that one of skill in the art would have known of any specific uses, and therefore, the court concluded this alleged use was too obscure to enable one of skill in the art to use the claimed invention. *See also Kawai v. Metlesics*, 480 F.2d 880, 178 USPQ 158 (CCPA 1973).

Kirk would potentially be dispositive of this case were the above-mentioned language the only assertion of utility found in the '944 application. Applicants' specification, however, also states that the claimed compounds have "a better action and a better action spectrum as antitumor substances" than known compounds, specifically those analyzed in Paull. As previously noted, *see supra* note 4, Paull grouped various benzo[de]isoquinoline-1,3-diones, which had previously been tested *in vivo* for antitumor activity against two lymphocytic leukemia tumor models (P388 and L1210), into various structural classifications and analyzed the test results of the groups (i.e. what percent of the compounds in the particular group showed success against the tumor models). Since one of the tested compounds, NSC 308847, was found to be highly effective against these two lymphocytic leukemia tumor models, [FN14] applicants' favorable comparison implicitly asserts that their claimed compounds are highly effective (i.e. useful) against lymphocytic leukemia. An alleged use against this particular type of cancer is much more specific than the vaguely intimated uses rejected by the courts in *Kirk* and *Kawai*. *See, e.g., Cross v. Iizuka*, 753 F.2d at 1048, 224 USPQ at 745 (finding the disclosed practical utility for the claimed compounds-the inhibition of thromboxane synthetase in human or bovine platelet microsomes-sufficiently specific to satisfy the threshold requirement in *Kirk* and *Kawai*.)

> FN14. Paull also found NSC 308847 to be effective against two other test models, B16 melanoma and Colon C872.

[2] The Commissioner contends, however, that P388 and L1210 are not diseases since the only way an animal can get sick from P388 is by a direct injection of the cell line. The Commissioner therefore concludes that applicants' reference to Paull in their specification does not provide a specific disease against which the claimed compounds can be used. We disagree.

As applicants point out, the P388 and L1210 cell lines, though technically labeled tumor models, were originally derived from lymphocytic leukemias in mice. Therefore, the P388 and L1210 cell lines do represent actual specific lymphocytic tumors; these models will produce this particular disease once implanted in mice. If applicants were required to wait until an animal naturally developed this specific tumor before testing the effectiveness of a compound against the tumor ***in vivo,*** as would be implied from the Commissioner's argument, there would be no effective way to test compounds ***in vivo*** on a large scale.

We conclude that these tumor models represent a specific disease against which the claimed compounds are alleged to be effective. Accordingly, in light of the explicit reference to Paull, applicants' specification alleges a sufficiently specific use.

2.

[3][4] The second basis for the Board's rejection was that, even if the specification did allege a specific use, applicants failed to ***1566** prove that the claimed compounds are useful. Citing various references,[FN15] the Board found, and the Commissioner now argues, that the tests offered by the applicants to prove utility

were inadequate to convince one of ordinary skill in the art that the claimed compounds are useful as antitumor agents.[FN16]

> FN15. *See* Pazdur et al., *Correlation of Murine Antitumor Models in Predicting Clinical Drug Activity in Non-Small Cell Lung Cancer: A Six Year Experience,* 3 Proceedings Am.Soc.Clin.Oncology 219 (1984); Martin et al., *Role of Murine Tumor Models in Cancer Research,* 46 Cancer Research 2189 (April 1986).

> FN16. As noted, this would appear to be a § 101 issue, rather than § 112.

This court's predecessor has stated:

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). From this it follows that the PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. *Id.* at 224, 169 USPQ at 370. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility. *See In re Bundy,* 642 F.2d 430, 433, 209 USPQ 48, 51 (CCPA 1981).[FN17]

> FN17. *See also In re Novak,* 306 F.2d 924, 928, 134 USPQ 335, 337 (CCPA 1962) (stating that it is proper for the examiner to request evidence to substantiate an asserted utility unless one with ordinary skill in the art would accept the allegations as obviously valid and correct); *In re Chilowsky,* 229 F.2d 457, 462, 108 USPQ 321, 325 (CCPA 1956) ("[W]here the mode of operation alleged can be readily understood and conforms to the known laws of physics and chemistry ... no further evidence is required."). *But see In re Marzocchi,* 439 F.2d at 223, 169 USPQ at 369-70 ("In the field of chemistry generally there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles.").

[5] The PTO has not met this initial burden. The references cited by the Board, Pazdur and Martin,[FN18] do not question the usefulness of any compound as an antitumor agent or provide any other evidence to cause one of skill in the art to question the asserted utility of applicants' compounds. Rather, these references merely discuss the therapeutic predictive value of *in vivo* murine tests-relevant only if applicants must prove the ultimate value in humans of their asserted utility. Likewise, we do not find that the nature of applicants' invention alone would cause one of skill in the art to reasonably doubt the asserted usefulness.

> FN18. *See supra* note 15.

The purpose of treating cancer with chemical compounds does not suggest an inherently unbelievable undertaking or involve implausible scientific principles. *In re Jolles,* 628 F.2d at 1327, 206 USPQ at 890. Modern science has previously identified numerous successful chemotherapeutic agents. In addition, the prior art, specifically Zee Cheng et al., discloses structurally similar compounds to those claimed by the applicants which have been proven *in vivo* to be effective as chemotherapeutic agents against various tumor models.

Taking these facts-the nature of the invention and the PTO's proffered evidence-into consideration we conclude that one skilled in the art would be without basis to reasonably doubt applicants' asserted utility on its face. The PTO thus has not satisfied its initial burden. Accordingly, applicants should not have been required to substantiate their presumptively correct disclosure to avoid a rejection under the first paragraph of § 112. *See In re Marzocchi,* 439 F.2d at 224, 169 USPQ at 370.

[6] We do not rest our decision there, however. Even if one skilled in the art ***1567** would have reasonably questioned the asserted utility, i.e., even if the PTO met its initial burden thereby shifting the burden to the applicants to offer rebuttal evidence, applicants proffered sufficient evidence to convince one of skill in the art of the asserted utility. In particular, applicants provided through Dr. Kluge's declaration [FN19] test results showing that several compounds within the scope of the claims exhibited significant antitumor activity against the L1210 standard tumor model ***in vivo.*** Such evidence alone should have been sufficient to satisfy applicants' burden.

> FN19. The declaration of Michael Kluge was signed and dated June 19, 1991. This declaration listed test results (i.e. antitumor activity) of the claimed compounds, *in vivo*, against L1210 tumor cells and concluded that these compounds would likely be clinically useful as anti-cancer agents. Enablement, or utility, is determined as of the application filing date. *In re Glass*, 492 F.2d 1228, 1232, 181 USPQ 31, 34 (CCPA 1974). The Kluge declaration, though dated after applicants' filing date, can be used to substantiate any doubts as to the asserted utility since this pertains to the accuracy of a statement already in the specification. *In re Marzocchi*, 439 F.2d at 224 n. 4, 169 USPQ at 370 n. 4. It does not render an insufficient disclosure enabling, but instead goes to prove that the disclosure was in fact enabling when filed (i.e., demonstrated utility).

[7] The prior art further supports the conclusion that one skilled in the art would be convinced of the applicants' asserted utility. As previously mentioned, prior art-Zee Cheng et al. and Paull-disclosed structurally similar compounds which were proven ***in vivo*** against various tumor models to be effective as chemotherapeutic agents. Although it is true that minor changes in chemical compounds can radically alter their effects on the human body, *Kawai*, 480 F.2d at 891, 178 USPQ at 167, evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility. *See Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 181 USPQ 453 (CCPA 1974); *Kawai*, 480 F.2d 880, 178 USPQ 158.

The Commissioner counters that such *in vivo* tests in animals are only preclinical tests to determine whether a compound is suitable for processing in the second stage of testing, by which he apparently means *in vivo* testing in humans, and therefore are not reasonably predictive of the success of the claimed compounds for treating cancer in humans.[FN20] The Commissioner, as did the Board, confuses the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption. *See Scott v. Finney*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed.Cir.1994) ("Testing for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings.").

> FN20. We note that this discussion is relevant to the earlier discussion as well. If we were to conclude that these *in vivo* tests are insufficient to establish usefulness for the claimed compounds, that would bear on the issue of whether one skilled in the art would, in light of the structurally similar compounds in Paull and Zee Cheng et al., have cause to doubt applicants' asserted usefulness for the compounds.

Our court's predecessor has determined that proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility. *In re Krimmel*, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961); *see also In re Bergel*, 292 F.2d 958, 130 USPQ 205 (CCPA 1961). In concluding that similar *in vivo* tests were adequate proof of utility the court in *In re Krimmel* stated:

> We hold as we do because it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment in humans.

Krimmel, 292 F.2d at 953, 130 USPQ at 219. Moreover, NCI apparently believes these tests are statistically significant because it has explicitly rec-

ognized both the P388 and L1210 murine tumor models as standard screening tests for determining whether new ***1568** compounds may be useful as antitumor agents.

In the context of this case the Martin and Pazdur references, on which the Commissioner relies, do not convince us otherwise. Pazdur only questions the reliability of the screening tests against lung cancer; it says nothing regarding other types of tumors. Although the Martin reference does note that some laboratory oncologists are skeptical about the predictive value of ***in vivo*** murine tumor models for human therapy, Martin recognizes that these tumor models continue to contribute to an increasing human cure rate. In fact, the authors conclude that this perception (i.e. lack of predictive reliability) is not tenable in light of present information.

On the basis of animal studies, and controlled testing in a limited number of humans (referred to as Phase I testing), the Food and Drug Administration may authorize Phase II clinical studies. *See* 21 U.S.C. § 355(i)(1); 21 C.F.R. § 312.23(a)(5), (a)(8) (1994). Authorization for a Phase II study means that the drug may be administered to a larger number of humans, but still under strictly supervised conditions. The purpose of the Phase II study is to determine primarily the safety of the drug when administered to a larger human population, as well as its potential efficacy under different dosage regimes. *See* 21 C.F.R. § 312.21(b).

[8] FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. *Scott*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

In view of all the foregoing, we conclude that applicants' disclosure complies with the requirements of 35 U.S.C. § 112 ¶ 1.

3.

[9] The Commissioner takes this opportunity to raise the question of this court's standard of review when deciding cases on appeal from the PTO. Traditionally we have recited our standard of review to be, with regard to questions of law, that review is without deference to the views of the Agency, *In re Donaldson*, 16 F.3d 1189, 1192, 29 USPQ2d 1845, 1848 (Fed.Cir.1994) (in banc), *In re Caveney*, 761 F.2d 671, 674, 226 USPQ 1, 3 (Fed.Cir.1985), and with regard to questions of fact, we defer to the Agency unless its findings are "clearly erroneous." *See, e.g., In re Baxter Travenol Labs*, 952 F.2d 388, 21 USPQ2d 1281 (Fed.Cir.1991); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed.Cir.1990); *In re De Blauwe*, 736 F.2d 699, 222 USPQ 191 (Fed.Cir.1984).

[10] With regard to judgment calls, those questions that fall "[s]omewhere near the middle of the fact-law spectrum," this court has recognized "the falseness of the fact-law dichotomy, since the determination at issue, involving as it does the application of a general legal standard to particular facts, is probably most realistically described as neither of fact nor law, but mixed." *Campbell v. Merit Systems Protection Board*, 27 F.3d 1560, 1565 (Fed.Cir.1994). When these questions of judgment are before us, whether we defer, and the extent to which we defer, turns on the nature of the case and the nature of the judgment. *Id.* ("Characterization therefore must follow from an *a priori* decision as to whether deferring ... is sound judicial policy. We would be less than candid to suggest otherwise.").

The Commissioner contends that the appropriate standard of review for this court regarding questions of law, of fact, and mixed questions of law and fact, coming to us from the PTO is found in the Administrative Procedure Act (APA) at 5 U.S.C. § 706. The standard set out there is that "[t]he reviewing court shall ... hold unlawful and set aside agency action, findings, and conclusions found to be-(A) arbitrary, capricious, an ***1569** abuse of discretion, or otherwise not in accordance with law; ... (E) unsupported by substantial evidence...." The Commissioner is of the view that the stated standard we now use, which is the traditional standard of review for matters coming from a trial court, is not appropriate for decisions coming from an agency with presumed expertise in the subject

area, and is not in accord with law.[FN21]

> FN21. Congress enacted the Administrative Procedure Act (APA) on June 11, 1946. *See* 1 Kenneth Culp Davis, Administrative Law Treatise, § 1:7 (2d ed. 1978). The APA sets forth a framework for administrative agency procedure and provides judicial review for persons adversely affected by final agency actions. Chapter 7, codified at 5 U.S.C. § 701-706, contains the APA judicial review provisions, including the standard of review provision quoted above.

Applicants argue that by custom and tradition, recognized by the law of this court, the standard of review we have applied, even though inconsistent with the standard set forth in the APA, nevertheless is a permissible standard. In our consideration of this issue, there is a reality check: would it matter to the outcome in a given case which formulation of the standard a court articulates in arriving at its decision? The answer no doubt must be that, even though in some cases it might not matter, in others it would, otherwise the lengthy debates about the meaning of these formulations and the circumstances in which they apply would be unnecessary.

A preliminary question, then, is whether this is one of those cases in which a difference in the standard of review would make a difference in the outcome. The ultimate issue is whether the Board correctly applied the § 112 ¶ 1 enablement mandate and its implicit requirement of practical utility, or perhaps more accurately the underlying requirement of § 101, to the facts of this case. As we have explained, the issue breaks down into two subsidiary issues: (1) whether a person of ordinary skill in the art would conclude that the applicants had sufficiently described particular diseases addressed by the invention, and (2) whether the Patent Act supports a requirement that makes human testing a prerequisite to patentability under the circumstances of this case.

The first subsidiary issue, whether the application adequately described particular diseases, calls for a judgment about what the various representations and discussions contained in the patent application's specification would say to a person of ordinary skill in the art. We have considered that question carefully, and, for the reasons we explained above in some detail, we conclude that the Board's judgment on this question was erroneous. Our conclusion rests on our understanding of what a person skilled in the art would gather from the various art cited, and from the statements in the application itself. We consider the Board's error to be sufficiently clear that it is reversible whether viewed as clear error or as resulting in an arbitrary and capricious decision.

The second subsidiary issue, whether human testing is a prerequisite to patentability, is a pure question of law: what does the practical utility requirement mean in a case of this kind. Under either our traditional standard or under the APA standard no deference is owed the Agency on a question of law, and none was accorded.

If the question concerning the standard of review, raised by the Commissioner, is to be addressed meaningfully, it must arise in a case in which the decision will turn on that question, and, recognizing this, the parties fully brief the issue. This is not that case. We conclude that it is not necessary to the disposition of this case to address the question raised by the Commissioner; accordingly, we decline the invitation to do so.

III. CONCLUSION

The Board erred in affirming the examiner's rejection under 35 U.S.C. § 112 ¶ 1. The decision is reversed.

REVERSED.

C.A.Fed.,1995.
In re Brana
51 F.3d 1560, 63 USLW 2656, 34 U.S.P.Q.2d 1436

END OF DOCUMENT

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H
This case was not selected for publication in the Federal Reporter.

Not for Publication in West's Federal Reporter See Fed. Rule of Appellate Procedure 32.1 generally governing citation of judicial decisions issued on or after Jan. 1, 2007. See also Federal Circuit Rule 32.1 and Federal Circuit Local Rule 32.1. (Find CTAF Rule 32.1)

United States Court of Appeals,
Federal Circuit.
ELI LILLY AND COMPANY, Plaintiff–Appellant,
v.
ACTAVIS ELIZABETH LLC, Defendant–Appellee,
and
Sun Pharmaceutical Industries, Ltd., Defendant–Appellee,
and
Sandoz, Inc., Defendant–Appellee,
and
Mylan Pharmaceuticals Inc., Defendant–Appellee,
and
Apotex Inc., Defendant–Appellee,
and
Aurobindo Pharma Ltd., Defendant–Appellee,
and
Teva Pharmaceuticals USA, Inc., Defendant–Appellee.

No. 2010–1500.
July 29, 2011.
Rehearing En Banc Denied Oct. 18, 2011.

Background: Holder of patent for use of compound atomoxetine to treat attention-deficit/hyperactivity disorder (ADHD) brought patent infringement action after competitors, which sought to market generic version of drug, filed abbreviated new drug applications (ANDAs) accompanied by Hatch–Waxman Act paragraph IV certification challenging patent's validity and enforceability and asserting non-infringement. On partial summary judgment, 676 F.Supp.2d 352, for which reconsideration was denied, 2010 WL 715411, and following bench trial, 731 F.Supp.2d 348, the United States District Court for the District of New Jersey, Dennis M. Cavanaugh, J., sustained patent against challenges of inequitable conduct, anticipation, obviousness, and non-enablement, but held patent claims invalid for lack of utility, and also ruled that, if claims were valid, defendants would be liable for inducement to infringe, but not contributory infringement. Patent holder appealed.

Holdings: The Court of Appeals, Newman, Circuit Judge, held that:
(1) patent was not invalid on ground of obviousness;
(2) full scope of patent claims was enabled;
(3) patent was not invalid for lack of enablement/utility;
(4) competitors' provision of atomoxetine labeled solely for use to treat ADHD constituted inducement to infringe patent; and
(5) competitors were liable for contributory infringement.

Affirmed in part, reversed in part, and remanded.

West Headnotes

[1] Patents 291 16.25

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.25 k. Chemical compounds. Most Cited Cases

Patent for use of compound atomoxetine to treat attention-deficit/hyperactivity disorder (ADHD) was not invalid on ground of obviousness where there was no evidence that use of atomoxetine had been identified as possible solution to problems of treating ADHD, nor that exercise of common sense would have led person of ordinary skill to test atomoxetine for treatment of ADHD, and evidence was contrary to likelihood that atomoxetine would be effective to treat ADHD, since atomoxetine was known not to be effective antidepressant and known norepinephrine inhibitor despiramine was associated with sudden death in children.

[2] Patents 291 99

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291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Full scope of claims of patent for use of compound atomoxetine to treat attention-deficit/hyperactivity disorder (ADHD) was enabled, despite competitors' assertion that formulations and dosages for treatment of ADHD were not routine and undue experimentation would be required to determine specific formulation and effective amount to be administered to particular patient, since known procedures for determination of appropriate dosages and formulation applied.

[3] Patents 291 49

291 Patents
291II Patentability
291II(C) Utility
291k49 k. Evidence of utility. Most Cited Cases

Patent for use of compound atomoxetine to treat attention-deficit/hyperactivity disorder (ADHD) satisfied utility requirement for validity, even though specification did not contain experimental data showing results of treatment of ADHD, where utility of atomoxetine was accurately stated and fully described in specification, there was no allegation of falsity in disclosed utility, experimental verification was obtained before patent was granted, and patent examiner did not require presentation of additional data.

[4] Patents 291 259(1)

291 Patents
291XII Infringement
291XII(A) What Constitutes Infringement
291k259 Contributory Infringement; Inducement
291k259(1) k. In general. Most Cited Cases

Competitors' provision of atomoxetine labeled solely for use to treat attention-deficit/hyperactivity disorder (ADHD) constituted inducement to infringe patent for use of compound atomoxetine to treat ADHD.

[5] Patents 291 259(1)

291 Patents
291XII Infringement
291XII(A) What Constitutes Infringement
291k259 Contributory Infringement; Inducement
291k259(1) k. In general. Most Cited Cases

Competitors marketing generic version of drug were liable for contributory infringement of patent for use of compound atomoxetine to treat attention-deficit/hyperactivity disorder (ADHD), which was only authorized use of atomoxetine, even if physicians could prescribe atomoxetine for unauthorized uses, since competitors were restricted from selling federally regulated drug for unapproved uses. 35 U.S.C.A. § 271(c); 21 C.F.R. § 202.1(e)(4).

Patents 291 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original utility. Most Cited Cases

4,314,081. Cited.

Patents 291 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original utility. Most Cited Cases

5,658,590. Valid and Infringed.

***918** Appeal from the United States District Court for the District of New Jersey, No. 07–CV–3770, Dennis M. Cavanaugh, Judge.Charles E. Lipsey, Finnegan, Henderson, Farabow, Garrett & Dunner, LLP, of Reston, VA, argued for the plaintiff-appellant. With

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him on the brief were L. Scott Burwell; Robert D. Bajefsky, Laura P. Masurovsky, and J. Derek McCorquindale, of Washington, DC; and Jennifer S. Swan, of Palo Alto, CA. Of counsel on the brief were Mark J. Stewart and Tonya L. Combs, Eli Lilly and Company, of Indianapolis, IN.

William A. Rakoczy, Rokaczy Molino Mazzochi Siwik LLP, of Chicago, IL, argued for defendants-appellees Sun Pharmaceutical Industries Ltd, Sandoz Inc. and Aurobindo Pharma, Ltd. With him on the brief for defendant-appellee Aurobindo Pharam Ltd was Christine J. Siwik. of counsel were Gregory A. Duff and Robert M. Teigen. On the brief were Keith V. Rockey and Kathleen A. Lyons, Rockey Depke, & Lyons, LLP, of Chicago, IL, for defendant-appellee Sandoz Inc.; and Thomas J. Parker and Victoria E. Spataro, Alston & Bird LLP, of New York, NY, for defendant-appellee Mylan Pharmaceuticals Inc.; Alan B. Clement, Hugh S. Balsam, Keith D. Parr, Andrea L. Wayda, Scott, B. Feder, Kevin M. Nelson and ***919**Myoka K. Goodin, Locke Lord Bissell & Liddell LLP, of New York, NY, for defendant-appellee Apotex, Inc. Of counsel on the brief was Shashank Upadhye, Apotex, Inc, of Toronto, Canada, for defendant-appellee Apotex, Inc. Also on the brief were James F. Hurst, Gail Standish, Peter E. Perkowski and Andrew C. Nichols, Winston & Strawn LLP, of Chicago, IL, for defendant-appellee Sun Pharamaceutical Industries, Ltd. Of counsel was Steffen Johnson.

Chad A. Landmon, Axinn, Veltop & Harkrider LLLP, of Hartford, CT, for defendant-appeelle Actavis Elizabeth LLC. With him on the brief was Matthew J. Becker.

Before NEWMAN, FRIEDMAN,[FN*] and LOURIE, Circuit Judges.

FN* Circuit Judge Friedman heard oral argument in this appeal, but died on July 6, 2011 and did not participate in the final decision. The case was decided by the remaining judges of the panel, in accordance with Fed. Cir. Rule 47.11.

NEWMAN, Circuit Judge.

****1** This case arises on the filing by each of the defendants of an Abbreviated New Drug Application (ANDA), accompanied by a Hatch–Waxman Act "Paragraph IV certification" challenging the validity and enforceability and asserting non-infringement of United States Patent No. 5,658,590 (the '590 patent) owned by Eli Lilly and Company. The '590 patent is directed to the use of the drug atomoxetine to treat attention-deficit/hyperactivity disorder (ADHD). Lilly obtained federal regulatory approval from the Food and Drug Administration (FDA), and markets the product for this use, with the brand name Strattera®. The defendants seek to sell generic counterparts of this drug before the expiration date of the '590 patent.

The United States District Court for the District of New Jersey sustained the '590 patent against the defendants' challenges on the grounds of inequitable conduct, anticipation, obviousness, and non-enablement. However, the court held the claims invalid for lack of utility, which the court called "enablement/utility." The court also held that if the claims were valid the defendants would be liable for inducement to infringe, but that they would not be liable for contributory infringement. The ruling of invalidity for lack of utility, and the ruling that contributory infringement does not also apply, are reversed. The district court's other rulings are affirmed.[FN1]

FN1. *Eli Lilly & Co. v. Actavis Elizabeth LLC*, 676 F.Supp.2d 352 (D.N.J.2009); 731 F.Supp.2d 348 (D.N.J.2010).

I

THE PATENTED INVENTION

The '590 patent is directed to the use of the compound tomoxetine,[FN2] having the chemical name (R)–(–)–N–methyl–3–(2–methylphenoxy)–3–phenyl propylamine, for treatment of ADHD. Claim 1 is as follows:

FN2. The common names "atomoxetine" and "tomoxetine" are both used in the record, and are used herein as they appear in the record.

1. A method of treating attention-deficit/hyperactivity disorder comprising administering to a patient in need of such treatment an effective amount of tomoxetine.

Claim 1 was treated by the parties and the district court as dispositive of the issues. At the time the '590 patent application was filed, tomoxetine was a known compound, described and claimed in Lilly's U.S. Patent No. 4,314,081, issued February 2, 1982. Tomoxetine was studied through Phase II clinical

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trials for the treatment of urinary incontinence, and through Phase III clinical trials for treatment of depression. *See* ***920** 21 C.F.R. § 312.21 (explaining Phase I, Phase II, and Phase III clinical trial criteria). Although the clinical trials showed that tomoxetine was safe for human use, the product did not provide the medicinal benefits for which it was being evaluated.

In 1993 Lilly scientists Dr. John Heiligenstein and Dr. Gary Tollefson suggested that tomoxetine might be effective for treatment of ADHD. ADHD is a complex neurobiological disorder characterized by developmentally inappropriate levels of inattention, hyperactivity, and impulsiveness. The district court explained that the occurrence of ADHD is wide, the cause is unknown, and the mechanism of drug treatment is unclear. *Eli Lilly,* 731 F.Supp.2d at 352–53, 366. It was explained at the trial that research concerning ADHD is difficult because there is no animal model for experimental evaluation of the effect of any particular treatment.

****2** At the time of this invention, all of the products that were being used to treat ADHD exhibited deficiencies. The '590 patent explains that the stimulants that were being used require multiple doses per day, produce a rebound effect between doses, and cause undesirable side effects; and the tricyclic antidepressants that were being used also produce undesirable side effects, and require careful supervision and dosage titration. The record states that the suggestion of Drs. Heiligenstein and Tollefson that tomoxetine might be an effective treatment for ADHD was met with skepticism. However, arrangements were made to conduct clinical tests at Massachusetts General Hospital, and on December 1, 1994 the investigators submitted to the FDA an Investigational New Drug (IND) application for treatment of ADHD with tomoxetine. On January 3, 1995 the FDA authorized the investigation. The ' 590 patent application was filed on January 11, 1995, and the clinical investigation commenced. By May 1995 initial positive results were obtained, and in October 1995 the investigators reported their preliminary results at a meeting of the American Association of Child and Adolescent Psychiatry.

Clinical investigation continued over the next seven years, including treatment of patients of various ages and ADHD severity, determination of possible side effects and of the cumulative effect of treatment, the development and evaluation of formulations, schedules, and dosages, and other studies relevant to determination of efficacy and safety. On November 26, 2002 the FDA approved the use of tomoxetine for treatment of ADHD in adults, children, and adolescents, at dosages of 10, 18, 25, 40, and 60 mg/day of oral administration; on February 14, 2005 the FDA also approved dosages of 80 and 100 mg/day. The record states that the product has achieved wide use.

II
OBVIOUSNESS

[1] The defendants challenged patent validity on the ground of obviousness, arguing that atomoxetine was a known norepinephrine inhibitor and thus that it would have been obvious to test this product for treatment of ADHD. The defendants argued that the inventors simply "substituted one potent selective norepinephrine reuptake inhibitor (atomoxetine) for another (desipramine) known to be effective in treating ADHD." *Eli Lilly*, 731 F.Supp.2d at 356 (quoting Defendants' Post–Trial Brief, at 7).

The district court, discussing this argument, referred to the reports of sudden death of children taking desipramine, and found that these "negative reports concerning desipramine .... must weigh to some extent away from using atomoxetine ***921** as a potential ADHD treatment" although "desipramine was functionally a similar compound to atomoxetine." *Id.* at 365. The court found that "while the prior art demonstrated that norepinephrine reuptake inhibition was relevant to ADHD treatment, the literature does not appear to indicate that it was alone sufficient." *Id.* at 362. The court stated that "it is impermissible to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *Id.* at 365–66 (quoting *In re Wesslau*, 53 C.C.P.A. 746, 353 F.2d 238, 241 (CCPA 1965)).

****3** The district court observed that the entirety of the prior art must be considered in determining obviousness. There was no evidence that the advantageous and effective properties of atomoxetine to treat ADHD, devoid of the negative effects of known and similar products, would have been obvious from the prior art. The district court found that treatment of ADHD with atomoxetine would not have been predicted by skilled

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artisans with a reasonable degree of certainty, and concluded that there was not clear and convincing evidence that the effective use of atomoxetine to treat ADHD would have been obvious to a person of ordinary skill in the field of the invention.

The defendants argue that, at the very least, it would have been "obvious to try" atomoxetine for this use. However, applying the guidance of *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S.Ct. 1727, 167 L.Ed.2d 705 (2007), there was no evidence that use of atomoxetine had been identified as a possible solution to the problems of treating ADHD, nor that the exercise of common sense would have led a person of ordinary skill to test atomoxetine for treatment of ADHD. *See id.* at 420–21, 127 S.Ct. 1727. The evidence was contrary to the likelihood that atomoxetine would be effective to treat ADHD, for atomoxetine was known not to be an effective antidepressant, and the known norepinephrine inhibitor despiramine was associated with sudden death in children. The experts for both sides were in agreement that they would not have expected that atomoxetine would be a successful treatment of ADHD.

We discern no error in the district court's ruling that the claims had not been proved invalid on the ground of obviousness.

III
ENABLEMENT/SCOPE

[2] The defendants argue that the '590 specification does not enable the full scope of claim 1, pointing out that the claim's words "administering to the patient an effective amount" are not limited to the formulations that are specifically exemplified in the specification. The defendants argue that the patent enables only the immediate release products and dosages in the specific examples, and that claim 1 is invalid because it is not so limited. The defendants' expert witness testified that formulations and dosages for treatment of ADHD are not routine, and thus that undue experimentation would be required to determine the specific formulation and effective amount to be administered to a specific patient.

The '590 patent describes the formulation and administration of tomoxetine as follows:

> Since tomoxetine is readily orally absorbed and requires only once/day administration, there is little or no reason to administer it in any other way than orally. It may be produced in the form ***922** of a clean, stable crystal, and thus is easily formulated in the usual oral pharmaceutical forms, such as tablets, capsules, suspensions, and the like. The usual methods of pharmaceutical scientists are applicable. It may be usefully administered, if there is any reason to do so in a particular circumstance, in other pharmaceutical forms, such as injectable solutions, depot injections, suppositories and the like, which are well known to and understood by pharmaceutical scientists. It will substantially always be preferred, however, to administer tomoxetine as a tablet or capsule and such pharmaceutical forms are recommended.

****4** '590 patent, col. 2 ll.20–33. The patent's description of dosages for treatment of ADHD with tomoxetine includes:

> The effective dose of tomoxetine for ADHD is in the range from about 5 mg/day to about 100 mg/day. The preferred adult dose is in the range from about 10 to about 80 mg/day, and a more highly preferred adult dose is from about 20 to about 60 mg/day. The children's dose of course is smaller, in the range from about 5 to about 70 mg/day, more preferably from about 10 to about 50 mg/day. The optimum dose for each patient, as always, must be set by the physician in charge of the case, talking into account the patient's size, other medications which the patient requires, severity of the disorder and all of the other circumstances of the patient.

Id. at col. 2 ll.7–19.

The district court found that "the various conceivable formulations are standard—and they were not part of the basis for the invention's patentability." *Eli Lilly*, 731 F.Supp.2d at 375. The court observed that the particular dosage form is not the invention, and is routinely determined:

> a dosage formulator as defined by the parties—a scientist with at least a bachelor's degree in pharmacy or some closely related field, at least three to five years of work experience in developing a particular pharmaceutical dosage form, and the ability to consult with others skilled in other particular disciplines (e.g., physicians, analytical chemists, and biopharmaceutical scientists)—would be able to do so without undue experimentation.

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Id. at 376. In *In re Wands*, 858 F.2d 731 (Fed.Cir.1988), this court identified several factors that may assist in determining whether experimentation is "undue":

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

858 F.2d at 737. The district court applied this precedent, and concluded that "reliance on formulation-related disclosures in the prior art [is] appropriate." *Eli Lilly*, 731 F.Supp.2d at 375.

The defendants cite *ALZA Corp. v. Andrx Pharmaceuticals LLC*, 603 F.3d 935 (Fed.Cir.2010), in which this court found that the patent did not "provide sufficient guidance for a person of ordinary skill in the art to make the nonosmotic dosage forms as claimed." *Id.* at 940. However, in that case the court described the field of ascending release dosage forms as "not mature" and "a 'breakaway' from the prior art." *Id.* at 941. Such characteristics were not here demonstrated. There was no evidence that known procedures for determination of dosages and formulation did not apply. *See* ***923***Spectra–Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed.Cir.1987) ("A patent need not teach, and preferably omits, what is well known in the art.").

****5** Enablement is not negated if a reasonable amount of experimentation is required to establish dosages and formulation of an active ingredient. *See Enzo Biochem, Inc. v. Calgene Inc.*, 188 F.3d 1362, 1371 (Fed.Cir.1999). Lack of enablement must be proved by clear and convincing evidence. *Auto. Tech. Int'l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274, 1281 (Fed.Cir.2007). Error has not been shown in the district court's finding and conclusion that the scope of the claims is enabled. That ruling is affirmed.

IV
ENABLEMENT/UTILITY

[3] The district court held all of the '590 patent claims invalid for lack of "enablement/utility." The court held that utility was not established because experimental data showing the results of treatment of ADHD were not included in the specification. The court held that "the court cannot conclude that a person of skill in the art would have recognized the method of treatment's utility in view of the specification and prior art." *Eli Lilly*, 731 F.Supp.2d at 389.

The patent statute requires that the specification "disclose as a matter of fact a practical utility for the invention." *In re Ziegler*, 992 F.2d 1197, 1201 (Fed.Cir.1993). Lilly points out that the utility to treat ADHD was fully disclosed and correctly described and enabled in the specification. The ' 590 patent describes the use of tomoxetine to treat ADHD in humans, and states that "tomoxetine is a notably safe drug, and its use in ADHD, in both adults and children, is a superior treatment for that disorder because of improved safety." Col.1 ll.66 to col.2 l.1. The patent refers to the two recognized types of ADHD, inattentive type and hyperactive-impulsive type, and states: "Treatment with tomoxetine is effective in patients who are primarily suffering from either component or from the combined disorder." Col.3 ll.38–40. The patent states:

> The method of the present invention is effective in the treatment of patients who are children, adolescents or adults, and there is no significant difference in the symptoms or the details of the manner of treatment among patients or different ages.

Col.4 ll.14–18. No criticism of the correctness of these statements has been offered. The defendants do not dispute that the '590 patent describes the utility of tomoxetine for treatment of ADHD, and that the utility is correctly described. Lilly agrees that human test data were not available at the time the patent application was filed, because human tests were prohibited without FDA authorization.

Dr. Heiligenstein, one of the inventors, testified about his uncertainty whether this treatment of ADHD would be effective, when he and Dr. Tollefson suggested experimental testing for this purpose:

> Q: At the time of this filing, did you have a reasonable expectation that tomoxetine would work to treat ADHD?
>
> A: It was a hypothesis.

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Q: Did you have a reasonable expectation?

A: Reasonable? Can you define reasonable?

****6** Q: Did you believe it was going to work for ADHD?

A: No, I wasn't sure at all that it would work.

Heiligenstein Dep. 127:4–12, August 7, 2008. It was not disputed that persons experienced in this field would require actual***924** human tests to verify the effectiveness of this use. As the Court discussed in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 593, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993): "Scientific methodology today is based on generating hypotheses and testing them to see if they can be falsified; indeed, this methodology is what distinguishes science from the other fields of human inquiry." (quoting Michael D. Green, 86 Nw. U.L.Rev. 643, 645 (1992)).

Although it was recognized that Dr. Heiligenstein's hypothesis required testing, Lilly points out that support for the testing was provided, patent procedures were initiated, and the FDA authorized proceeding with human clinical trials. The Manual of Patent Examining Procedure instructs examiners to give presumptive weight to the utility for which human trials have been initiated:

> MPEP § 2107.03 (8th ed.2008). IV.... Before a drug can *enter* human clinical trials, the sponsor, often the applicant, must provide a convincing rationale to those *especially* skilled in the art (e.g., the Food and Drug Administration) that the investigation may be successful. Such a rationale would provide a basis for the sponsor's expectation that the investigation may be successful. In order to determine a protocol for phase I testing, the first phase of clinical investigation, some credible rationale of how the drug might be effective or could be effective would be necessary. *Thus, as a general rule, if an applicant has initiated human clinical trials for a therapeutic product or process, Office personnel should presume that the applicant has established that the subject matter of that trial is reasonably predictive of having the asserted therapeutic utility.*

(Emphases in original.) During examination of the '590 application, the patent examiner did not require the submission of data showing treatment of ADHD with atomoxetine, although it is not disputed that such data were obtained shortly after the patent application was filed. The utility of this product to treat ADHD is not so incredible as to warrant the special procedures that are authorized for use when the examiner doubts the described utility, as in *In re Swartz*, 232 F.3d 862 (Fed.Cir.2000) (cold fusion); *Newman v. Quigg*, 877 F.2d 1575, *modified* 886 F.2d 329 (Fed.Cir.1989) (perpetual motion); and for subject matter in once notoriously intractable areas such as cures for baldness or cancer. In deciding whether additional information is required for examination purposes, deference is owed to the "qualified agency presumed to have properly done its job." *Am. Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350, 1359 (Fed.Cir.1984).

In this case, evidence of the described utility of tomoxetine was not requested by the patent examiner, although experimental verification was obtained soon after the filing of the patent application. The examination of the '590 patent was in accordance with the rules, as the court has explained:

> ****7** [A] specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented *must* be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter *unless* there is reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

In re Langer, 503 F.2d 1380, 1391 (CCPA 1974) (emphases in original). In *In re Brana*, 51 F.3d 1560 (Fed.Cir.1995) the court again explained that:

> A specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond to those used in describing and defining the subject matter ***925** sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

51 F.3d at 1566 (quoting *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 223 (CCPA 1971)) (emphases in original). In *Brana*, where the utility was

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antitumor activity in humans, the court reaffirmed the practice that: "Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility." *Id.* at 1566 (citing *In re Bundy*, 642 F.2d 430, 433 (CCPA 1981)). Such evidence was not here provided by the PTO, and rebuttal evidence was not required.

The district court's statement that "there was no credible disclosure of utility to begin with," *Eli Lilly*, 731 F.Supp.2d at 386 n. 18, does not comport with the specification's extensive disclosure of utility. The district court appears to have accepted the defendants' argument that in view of the absence of experimental data in the specification, the disclosed utility must be deemed incredible. The district court apparently also accepted the defendants' position that such data were required to be included in the specification. However, the purported authority cited by the defendants concerned quite different issues, where, for various reasons, it was appropriate to offer experimental evidence. For example, the district court relied on patent "interference" cases, as in *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1324 (Fed.Cir.2005), where evidence of actual reduction to practice was required to establish a priority date earlier than that of an adverse claimant.

When priority is not at issue, generally the applicant may provide data obtained either before or after the patent application was filed. With reference to demonstration of utility, in *Brana*, 51 F.3d at 1567 n. 19 the court noted that post-filing evidence "can be used to substantiate any doubts as to the asserted utility since this pertains to the accuracy of a statement already in the specification." Here, the utility of tomoxetine is accurately stated in the specification; there is no allegation of falsity in the disclosed utility, and the patent examiner did not require the presentation of additional data. In *In re Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220 (CCPA 1971) the court had explained that:

> ****8** The only relevant concern of the Patent Office under these circumstances should be over the truth of any such assertion. The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

439 F.2d at 223. The '590 patent describes and enables the utility of tomoxetine to treat ADHD. The disclosure is not "on its face, contrary to generally accepted scientific principles." *Id.* at 223. Lilly's expert testified that the utility of tomoxetine to treat ADHD "had not been ruled out," Trial Tr. 1099:4, and even the defendants' expert testified that "it could work." Trial Tr. 200:22.

The defendants rely on *Janssen Pharmaceutica N.V. v. Teva Pharmaceuticals USA, Inc.*, 583 F.3d 1317 (Fed.Cir.2009) where the court held that the use of galantamine to treat Alzheimer's disease was a "mere research proposal." The specification summarized six scientific articles on the properties of galantamine to raise blood levels of cortisol and ACTH, and reporting brain effects in mammals, and ***926** the court held that because the animal tests were "not finished ... by the time the '318 patent was allowed," enablement was not shown. The court held that there was not "a reasonable correlation between a compound's activity and its asserted therapeutic use," in the words of MPEP § 2107.03. In the case of atomoxetine, however, the norepinephrine relationship was known, safety for antidepressant activity had been established, the specification contained a full description of the utility, experimental verification had been obtained before the patent was granted, and the examiner had not requested additional information. There was no evidence that the disclosure is "on its face, contrary to generally accepted scientific principles." *Marzocchi*, 439 F.2d at 223. As stated in *Brana*, 51 F.3d at 1566–67: "Even if one skilled in the art would have reasonably questioned the asserted utility, i.e., even if the PTO met its initial burden thereby shifting the burden to the applicants to offer rebuttal evidence, applicants proffered sufficient evidence to convince one of skill in the art of the asserted utility."

On the entirety of the evidence, invalidity for lack of enablement/utility was not shown by clear and convincing evidence. The district court's holding of invalidity on this ground is reversed.

V
INFRINGEMENT

[4] The district court held that the defendants would be liable for inducement to infringe the '590

patent by providing atomoxetine bearing the FDA-approved label authorizing use to treat ADHD. The defendants argue that "the mere distribution of generic atomoxetine products cannot establish inducement liability, even though the labeling includes the legally required statement of FDA-approved use." Lilly responds that the label use to treat ADHD is the only legally approved use, and the only use for which the defendants are authorized to provide the product.

****9** The defendants rely on *Warner–Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed.Cir.2003), for its finding of noninfringement, although in that case the patent on the only FDA-authorized use had expired, and the court held that the provider of the generic product, labeled for the authorized use on which the patent had expired, did not infringe a different (unexpired) patent on an unauthorized use:

> [T]he request to make and sell a drug labeled with a permissible (non-infringing) use cannot reasonably be interpreted as an act of infringement (induced or otherwise) with respect to a patent on an unapproved use, as the ANDA does not induce anyone to perform the unapproved acts required to infringe.
>
> 316 F.3d at 1364–65.

The defendants also argue that there are off-label uses of atomoxetine, stated by the defendants to be as high as 29% of the total, and conceded by Lilly as possibly as high as 8% of the total. However, the product sold by the defendants is labeled solely for the patented use to treat ADHD. We have long held that the sale of a product specifically labeled for use in a patented method constitutes inducement to infringe that patent, and usually is also contributory infringement. *See Astrazeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed.Cir.2010) (finding intent to induce infringement based on the product label authorizing the patented use, which "would inevitably lead some consumers to practice the claimed method"); *see also DSU Med. Corp. v. JMS Co. Ltd.*, 471 F.3d 1293, 1305–06 (Fed.Cir.2006) (en banc in relevant part) (finding liability for induced infringement when an entity "offers a product with the object of promoting its use to ***927** infringe, as shown by clear expression or other affirmative steps taken to foster infringement").

No clear error has been shown in the district court's findings and conclusion regarding inducement. We affirm the judgment that the provision of atomoxetine labeled solely for use to treat ADHD constitutes inducement to infringe the ' 590 patent.

[5] As for contributory infringement, the district court held that liability is avoided if the product has any "frequent" non-infringing use. Lilly argues that atomoxetine is not a "staple article of commerce suitable for substantial noninfringing use," the words of 35 U.S.C. § 271(c), for the only authorized use of atomoxetine is the patented use to treat ADHD. The defendants are restricted from selling a federally regulated drug for unapproved uses. *See* 21 C.F.R. § 202.1(e)(4). The defendants respond that physicians may nonetheless prescribe atomoxetine for unauthorized use. Such unauthorized activity does not avoid infringement by a product that is authorized to be sold solely for the infringing use.

We conclude that the district court erred in its application of the law of contributory infringement. That aspect of the district court's decision is reversed.

SUMMARY

The judgment that the '590 patent claims are invalid for lack of "enablement/utility" is reversed. The district court's rulings of validity on other grounds, and the judgment of infringement, are affirmed. We remand for further proceedings.

****10 AFFIRMED–IN–PART, REVERSED–IN–PART, and REMANDED.**

C.A.Fed. (N.J.),2011.
Eli Lilly and Co. v. Actavis Elizabeth LLC
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END OF DOCUMENT

520 F.3d 1358, 86 U.S.P.Q.2d 1196
(Cite as: 520 F.3d 1358)

United States Court of Appeals,
Federal Circuit.
ORTHO-McNEIL PHARMACEUTICAL, INC.,
Plaintiff-Appellee,
v.
MYLAN LABORATORIES, INC., and Mylan Pharmaceuticals, Inc., Defendants-Appellants.

No. 2007-1223.
March 31, 2008.

Background: Patentee brought action against competitor alleging infringement of patent relating to chemical formula of anticonvulsive drug topiramate. The United States District Court for the District of New Jersey, Stanley R. Chesler, J., denied competitor's motion for summary judgment, 2005 WL 1683644, granted patentee's motions for partial summary judgment, 2006 WL 1517749, 2006 WL 2865469, 2007 WL 432792, and granted patentee's motion for entry of final judgment, 2007 WL 869545. Competitor appealed.

Holdings: The Court of Appeals, Rader, Circuit Judge, held that:
(1) term "and," in claim of patent, was used to connote alternatives rather than in the additive sense;
(2) patentee's statements about prior art references for chemical compounds made during patent prosecution were not misrepresentations;
(3) patent claims were not obvious; and
(4) patent specification disclosing that the average adult requires 30-2000 milligrams of claimed compounds administered in two to four doses at 10-500 milligrams adequately enabled claims of patent.

Affirmed.

West Headnotes

[1] Patents 291 101(2)

291 Patents
291IV Applications and Proceedings Thereon
291k101 Claims
291k101(2) k. Construction in general. Most Cited Cases

Term "and," in claim of patent relating to chemical formula of anticonvulsive drug topiramate, was used to connote alternatives rather than in the additive sense; "and" appeared in conjunction with adverbs "independently" and "together," and construing the claim to require a conjunctive meaning of "and" would have rendered several dependent claims meaningless.

[2] Patents 291 165(3)

291 Patents
291IX Construction and Operation of Letters Patent
291IX(B) Limitation of Claims
291k165 Operation and Effect of Claims in General
291k165(3) k. Construction of language of claims in general. Most Cited Cases

A nonsensical result does not require the court to redraft the claims of a patent.

[3] Patents 291 97.11

291 Patents
291IV Applications and Proceedings Thereon
291k97.7 Unenforceability of Patent; Inequitable Conduct or Fraud on Office
291k97.11 k. Misrepresentation of material fact. Most Cited Cases
(Formerly 291k97)

Patentee's statements about prior art references for chemical compounds made during patent prosecution of patent relating to anticonvulsive drug topiramate were not misrepresentations, despite argument that patentee's statements were inconsistent with its own information about the compounds; statements merely accurately characterized references as claiming limited utility for compounds, and made no assertions about the compounds themselves.

[4] Patents 291 16.25

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.25 k. Chemical compounds. Most Cited Cases

Claims for patent relating to anticonvulsive drug topiramate were not obvious; challenges of inventive process would have prevented one of ordinary skill in the art from traversing the multiple obstacles to easily produce the invention in light of the evidence available at the time of invention.

[5] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Specification of patent relating to chemical formula of anticonvulsive drug topiramate, disclosing that the average adult requires 30-2000 milligrams of the claimed compounds administered in two to four doses at 10-500 milligrams, adequately enabled claims of patent, despite argument that anticonvulsive effective amount was unclear and its determination would require undue experimentation.

[6] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

A patent specification that enables an invention will teach those ordinarily skilled in the art to make and use the full scope of the claimed invention without undue experimentation.

[7] Health 198H 319

198H Health
198HI Regulation in General
198HI(E) Drugs; Medical Devices and Instruments
198Hk315 Applications and Approvals
198Hk319 k. Generic and orphan drugs; market exclusivity. Most Cited Cases

Statute relating to Food and Drug Administration's (FDA) responsibilities in approving an abbreviated new drug application (ANDA) after finding a patent infringed does not limit a court's authority to reset the effective date of an ANDA for conditions other than those listed. Federal Food, Drug, and Cosmetic Act, § 505, 21 U.S.C.A. § 355; 35 U.S.C.A. § 271.

Patents 291 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original utility. Most Cited Cases

4,513,006. Infringed.

***1360** Harry J. Roper, Jenner & Block LLP, of Chicago, Illinois, argued for plaintiff-appellee. With him on the brief were Aaron A. Barlow and Eric L. Lohrenz, of Chicago, Illinois, and Marc A. Goldman, of Washington, DC.

David J. Harth, Heller Ehrman LLP, of Madison, Wisconsin, argued for defendants-appellants. With him on the brief were Randy J. Kozel, of Madison, Wisconsin, and Shannon M. Bloodworth, of Washington, DC.

Before MICHEL, Chief Judge, RADER and LINN, Circuit Judges.

RADER, Circuit Judge.

The United States District Court for the District of New Jersey permanently enjoined Mylan Laboratories, Inc. from infringing Ortho-McNeil Pharmaceutical Inc.'s U.S. Patent No. 4,513,006 ('006). The '006 patent claims the anticonvulsive drug topiramate. The trial court also reset the effective approval date for Mylan's Abbreviated New Drug Application (ANDA). Because the district court correctly ruled on claim construction, inequitable conduct, obviousness, and enablement, and because the district court did not err in resetting the effective date of Mylan's ANDA under 35 U.S.C. § 271(e)(4)(A), this court affirms.

520 F.3d 1358, 86 U.S.P.Q.2d 1196
(Cite as: 520 F.3d 1358)

I

Topiramate (marketed by Ortho-McNeil as TOPOMAX®) is a significant epilepsy drug with sales exceeding $1 billion annually. Ortho-McNeil scientist Dr. Bruce Maryanoff invented this pharmaceutical during a search for new antidiabetic drugs. Topiramate is a reaction intermediate in the synthesis Dr. Maryanoff ran as part of his antidiabetic efforts. Unexpectedly, Dr. Maryanoff discovered that this particular intermediate had powerful anticonvulsant properties. After extensive testing, clinical trials, and substantial investment, Ortho-McNeil showed that the compound was safe and effective leading to FDA approval.

This cause of action arose under the Hatch-Waxman Act. 21 U.S.C. § 355. Under that Act, Mylan filed an ANDA with the FDA with a paragraph IV certification asserting that Ortho-McNeil's '006 patent is invalid or not infringed. Within 45 days, Ortho-McNeil filed an infringement suit under 35 U.S.C. § 271(e)(2) against Mylan thus triggering the 30-month stay on approval of Mylan's ANDA.

After a Markman proceeding to set the meaning of the claim terms, the district court rejected Mylan's position that claim 1 of the '006 patent does not cover topiramate. Indeed, in light of the district court's claim construction ruling, Mylan stipulated that its generic topiramate infringes claims 1, 2, 4, 5, 6, 7, 8, 11 and 12 of the '006 patent. On summary judgment, the trial court also ruled against Mylan's affirmative defenses of unenforceability due to inequitable conduct and invalidity based on obviousness and non-enablement. After entry of final judgment, Mylan now appeals the district court's claim construction as well as the dismissal of its affirmative defenses of inequitable conduct, obviousness, and non-enablement.

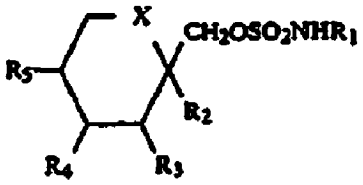
II

This court reviews a grant of summary judgment without deference. *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1353 (Fed.Cir.1998). This court must decide for itself "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 a judgment as a matter of law." Fed.R.Civ.P. 56(c); *Celotex Corp. v. Catrett*, 477 U.S. 317, 322, 106 S.Ct. 2548, 91 L.Ed.2d 265 (1986). In deciding these ***1361** questions, this court draws all justifiable inferences in the nonmovant's favor. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255, 106 S.Ct. 2505, 91 L.Ed.2d 202 (1986). This court also reviews claim construction as a matter of law without deference. *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1456 (Fed.Cir.1998) (en banc).

[1] Mylan argues that the district court improperly construed the word *and* to mean *or* in independent claim 1, and under the proper construction, the claim does not cover topiramate. In light of the plain language of independent claim 1, several dependent claims, the specification, and the extrinsic evidence, this court sustains the trial court's ruling that, in the circumstances of this case, claim 1's use of the term *and* means *or*.

Claim 1 of the '006 patent states:

1. A sulfamate of the following formula (I):



wherein

X is oxygen;

R1 is hydrogen or alkyl; and

R2, R3, R4 and R5 are independently hydrogen or lower alkyl and R2 and R3 and/or R4 and R5 together may be a group of the following formula (II):

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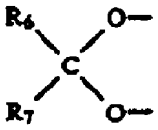
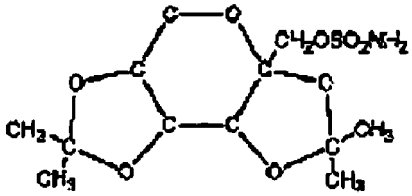


wherein

R6 and R7 are the same or different and are hydrogen, lower alkyl or are alkyl and are joined to form a cyclopentyl or cyclohexyl ring.

Topiramate has the following structure:



In the molecule topiramate, R2 and R3 and R4 and R5 together are a group of formula (II), wherein R6 and R7 are methyl. Mylan argues that the use of the term *and* precludes the claim from encompassing topiramate. In context, the term *and* falls between several R group recitations:

> R2, R3, R4, and R5 are independently hydrogen or lower alkyl *and* R2 and R3 and/or R4 and R5 together may be a group of formula (II) (emphasis added).

On this basis, Mylan argues that the phrase quoted above contains two independent claim limitations: (1) that "R2, R3, R4, and R5 are independently hydrogen or lower alkyl" *and* (2) that "R2 and R3 and/or R4 and R5 together may be a group of formula (II)." Under Mylan's construction, both of these limitations must be met in order for a compound to infringe. Both of these limitations are not met in topiramate. None of the R2, R3, R4, and R5 subunits are hydrogen or lower alkyl because both R2 and R3 and R4 and R5 together are a group of formula (II).

To the contrary, the claim language depicts two subsets of compounds, but does not require their simultaneous existence. In one subset of compounds covered by claim 1, the groups R2, R3, R4, and R5 are independent of one another, in which case, according to the claim, they are either hydrogen or lower alkyl. In a second subset of compounds covered by claim 1, ***1362** the R2 through R5 groups are not independent, but rather R2 and R3 are together, and/or R4 and R5 are together, to form either one or two groups of formula (II). Topiramate is an example of this type of compound. In it, R2 and R3 are arranged together in a group, as are R4 and R5. Thus, as used in this claim, *and* conjoins mutually exclusive possibilities.

The claim also does not use *and* in isolation but in a larger context that clarifies its meaning. Specifically, *and* appears in conjunction with the adverbs *independently* and *together*. As the district court explained, these terms signal that *and* links alternatives that occur under the different conditions of independence or togetherness. In context, it is clear that one of the subunits (R2, R3, R4, or R5) does not always have to be either a hydrogen or lower alkyl.

The larger context of this patent also supports this claim meaning. Construing claim 1 to require a conjunctive meaning of *and* would render several dependent claims meaningless. Claims 2, 5, 9, and 10 would cover nothing if the *and* at issue must be conjunctive. This court has explained: "Other claims of the patent in question ... can also be valuable sources of enlightenment as to the meaning of a claim term." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed.Cir.2005) (en banc) (citing *Vitronics Corp. v. Conceptronic Inc.*, 90 F.3d 1576, 1582 (Fed.Cir.2003)). Thus, this court strives to reach a claim construction that does not render claim language in dependent claims meaningless. *Rambus Inc. v. Infineon Tech. AG*, 318 F.3d 1081, 1093 (Fed.Cir.2003).

The specification also supports the district court's

reading of *and.* The specification thus uses the word *and* to link alternative chemical structures. In column 1 lines 47-50 the specification provides:

> R2, R3, R4 and R5 are independently hydrogen or lower alkyl *and,* when X is CH2, R4 and R5 may be alkene groups joined to form a benzene ring *and* when X is oxygen, R2 and R3 and/or R4 and R5 together may be a methylenedioxy group of the following formula II....

(emphases added). Without question, this passage within the specification shows use of the word *and* to join alternatives.

While extrinsic evidence "can shed useful light on the relevant art," this court considers such evidence "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.' " *Phillips,* 415 F.3d at 1317 (citations omitted). Because the plain language of claim 1, the dependent claims, and the specification support the district court's reading, this court does not need to consult extrinsic evidence. Nonetheless, this court notes that dictionary definitions of *and,* while most often listing the additive sense as the most common usage of the term, also show usage of the term to connote alternatives. *Webster's Third New International Dictionary* (2002). In the circumstances of this case, the use of *and* to express alternatives was chosen and adequately expressed by the applicant. Thus, extrinsic evidence too offers support for the district court's reading of the disputed term.

[2] In *Chef America Inc. v. Lamb Weston, Inc.,* this court explained that a patent must be interpreted "as written, not as the patentees wish they had written it." 358 F.3d 1371, 1374 (Fed.Cir.2004). In other words, courts may not redraft claims, whether to make them operable or to sustain their validity. *Id.* Even "a nonsensical result does not require the court to redraft the claims of the ... patent." *Id.* (citing *Process Control Corp. v. HydReclaim Corp.,* 190 F.3d 1350, 1357 (Fed.Cir.1999)). However, *Chef America* does not require this court or the district court to interpret *and* according to its most common***1363** usage in the dictionary. To the contrary, this court and the district court must interpret the term to give proper meaning to the claim in light of the language and intrinsic evidence. Giving *and* its most common dictionary meaning would produce in this case the nonsensical result of not covering topiramate and rendering several other dependent claims meaningless. In *Chef America,* the only possible interpretation of the claim led to a nonsensical result. This situation is distinguishable because claim 1 can and should be interpreted as the patentees intended, with the meaning of *and* connoting alternatives.

In sum, the district court properly interpreted the claim. This court detects no error in its claim construction.

III

[3] Mylan accuses Ortho-McNeil of committing inequitable conduct by failing to disclose the results of non-public tests it conducted on the prior art Kochetkov compounds to the Patent Office. In fact, the applicant submitted the Kochetkov references themselves, but not results from the tests that Dr. Maryanoff conducted on the compounds. Mylan says that Ortho-McNeil's statements about the Kochetkov references during prosecution were inconsistent with Ortho-McNeil's own information that the compounds had anticonvulsant properties. During prosecution, Ortho-McNeil said the following:

> It should be noted that the utility disclosed in the Kochetkov references AR-AU is extremely limited and narrow. These compounds are merely taught as being convenient derivatives of monosaccharide sulfates to allow separation of such sulfates from each other with regeneration of the original sulfate thereafter. No teaching is provided for any actual utility of the sulfamates or sulfates described in AR-AU and it is respectfully submitted that there is no motivation for one skilled in the art reading AR-AU to go beyond the pyranoses disclosed therein to arrive at Applicant's invention.

Mylan claims that this was a misrepresentation because in-house test results demonstrated that the Kochetkov compounds had anticonvulsive properties. To the contrary, the district court found, and this court agrees, that Ortho-McNeil did not make misrepresentations to the Patent Office during prosecution. The quoted passage merely accurately characterizes the references as claiming limited utility for the Kochetkov compounds. Ortho-McNeil made no assertions about the compounds themselves, but only repeated the disclosures of the Kochetkov references.

The same observation applies to the sentence following the passage quoted above:

> As explained above, the pyranoses of AR-AU are entirely different in structure and use than the pyranoses of the present invention, and given the minimal usefulness of the AR-AU compounds, it would not be obvious to one skilled in the art to go beyond AR-AU to the pyranose structures of the present invention.

Again, as the opening phrase of the above quote confirms, the applicant is repeating the disclosures of the Kochetcov references, not characterizing the compounds themselves. Read in context, the Kochetkov references do not disclose any utility. On this point, the applicant is correct. Moreover, the applicant did not assert that the compounds themselves possess no utility. Thus, Ortho-McNeil made no misrepresentations to the Patent Office. Accordingly the district court correctly dismissed Mylan's affirmative defense of inequitable conduct.

IV

[4] Dr. Laurens Anderson, Mylan's expert, asserts that a person of ordinary skill ***1364** in the art faced with finding a diabetes drug (as Dr. Maryannoff was) would necessarily design an FBPase inhibitor. Mylan cites *KSR International Co. v. Teleflex Inc.*, for the proposition that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." 550 U.S. 398, 127 S.Ct. 1727, 1742, 167 L.Ed.2d 705 (2007). The record, however, shows that even if an ordinarily skilled artisan sought an FBPase inhibitor, that person would not have chosen topiramate. Moreover this invention, contrary to Mylan's characterization, does not present a finite (and small in the context of the art) number of options easily traversed to show obviousness. The passage above in *KSR* posits a situation with a finite, and in the context of the art, small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness. In this case, the record shows that a person of ordinary skill would not even be likely to start with 2,3:4,5 di-isopropylidene fructose (DPF), as Dr. Maryanoff did. Beyond that step, however, the ordinarily skilled artisan would have to have some reason to select (among several unpredictable alternatives) the exact route that produced topiramate as an intermediate. Even beyond that, the ordinary artisan in this field would have had to (at the time of invention without any clue of potential utility of topiramate) stop at that intermediate and test it for properties far afield from the purpose for the development in the first place (epilepsy rather than diabetes). In sum, this clearly is not the easily traversed, small and finite number of alternatives that *KSR* suggested might support an inference of obviousness. *Id.* at 1742.

In other words, Mylan's expert, Dr. Anderson, simply retraced the path of the inventor with hindsight, discounted the number and complexity of the alternatives, and concluded that the invention of topiramate was obvious. Of course, this reasoning is always inappropriate for an obviousness test based on the language of Title 35 that requires the analysis to examine "the subject matter as a whole" to ascertain if it "*would have been obvious at the time the invention was made.*" 35 U.S.C. § 103(a) (emphasis added). In retrospect, Dr. Maryanoff's pathway to the invention, of course, seems to follow the logical steps to produce these properties, but at the time of invention, the inventor's insights, willingness to confront and overcome obstacles, and yes, even serendipity, cannot be discounted.

Speaking before *KSR*, the district court endorsed a "rigorous application" of the teaching, suggestion, or motivation (TSM) test. In *KSR*, the Supreme Court explained that a "rigid" TSM test "is incompatible with our precedents." *KSR*, 127 S.Ct. at 1741. Mylan thus contends that the district court erred by rigorously applying the TSM test. The Supreme Court explained its reason for castigating a "rigid" TSM test: "The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents." *Id.* Indeed a rigid requirement of reliance on written prior art or patent references would, as the Supreme Court noted, unduly confine the use of the knowledge and creativity within the grasp of an ordinarily skilled artisan. *Id.* at 1742.

As this court has explained, however, a flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis such as occurred in this case. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed.Cir.2007) ("[A]s the Supreme Court sug-

gests, a flexible approach***1365** to the TSM test prevents hindsight and focuses on evidence before the time of invention."). The TSM test, flexibly applied, merely assures that the obviousness test proceeds on the basis of evidence-teachings, suggestions (a tellingly broad term), or motivations (an equally broad term)-that arise before the time of invention as the statute requires. As *KSR* requires, those teachings, suggestions, or motivations need not always be written references but may be found within the knowledge and creativity of ordinarily skilled artisans.

In this case, the record amply supports the district court's finding of nonobviousness. This court detects no rigid application of the evidentiary requirements for obviousness in the district court's analysis. As noted above, the challenges of this inventive process would have prevented one of ordinary skill in this art from traversing the multiple obstacles to easily produce the invention in light of the evidence available at the time of invention. Of particular importance beyond the prima facie analysis, this court also detects evidence of objective criteria showing nonobviousness. Specifically, the record shows powerful unexpected results (anticonvulsive activity) for topiramate. The record also shows skepticism of experts and copying-other respected sources of objective evidence of nonobviousness-as well as commercial success. As this court has repeatedly explained, this evidence is not just a cumulative or confirmatory part of the obviousness calculus but constitutes independent evidence of nonobviousness. *Catalina Lighting, Inc. v. Lamps Plus, Inc.*, 295 F.3d 1277, 1288 (Fed.Cir.2002) ("Objective indicia may often be the most probative and cogent evidence of nonobviousness in the record.") (internal citation omitted). *See also PharmaStem Therapeutics Inc. v. Viacell, Inc.*, 491 F.3d 1342; *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369.

Mylan asserts that method of use claims 6-8 are also obvious. But if claim 1 is not obvious then claims 6-8 also cannot be obvious because they all depend from a nonobvious claim. *In re Fritch*, 972 F.2d 1260, 1266 (Fed.Cir.1992) ("[D]ependent claims are nonobvious if the independent claims from which they depend are nonobvious."). Accordingly, the method of use claims are nonobvious as well.

V

[5][6] Mylan asserts that claims 6-8 are not enabled because an *anticonvulsively effective* amount is unclear and its determination would require undue experimentation. A specification that enables an invention will teach those ordinarily skilled in the art to make and use the full scope of the claimed invention without undue experimentation. *Genentech Inc. v. Novo Nordisk of N. Am. Inc.*, 108 F.3d 1361, 1365 (Fed.Cir.1997).

The '006 specification discloses that the average adult requires 30-2000 milligrams of the claimed compounds administered in two to four doses of 10-500 milligrams. The specification also teaches a skilled artisan to use the claimed compounds in a manner similar to the drug phenytoin. Further the specification directs the reader to a reference by L.S. Goodman, which teaches that after establishment of a low initial dose, the dosage is increased at appropriate intervals as required for control of seizures or as limited by toxicity with further adjustments according to plasma drug concentrations. L.S. Goodman, et al., *The Pharmacological Basis of Therapeutics*, 201-26 (5th ed.1975). This court sustains the district court's judgment that this disclosure adequately enables claims 6-8. Further, even if clinical trials informed the anticonvulsively effective amount, this record does not show that extensive or "undue" tests would be required***1366** to practice the invention. The district court was correct in summarily dismissing Mylan's non-enablement defense.

VI

When a generic manufacturer files an ANDA with a paragraph IV certification, Hatch-Waxman grants the brand name pharmaceutical manufacturer a 30-month stay in the approval of that ANDA within which to litigate its case. 21 U.S.C. § 355(j)(5)(B)(iii). At the expiration of the 30 months, the ANDA is automatically approved unless the court grants a preliminary injunction or finds infringement. Because neither of those two events occurred before expiration of 30 months, the FDA approved Mylan's ANDA by operation of law. Therefore, after determining infringement, the district court reset the effective date of approval pursuant to 35 U.S.C. § 271(e)(4)(A), which provides:

> (4) For an act of infringement described in paragraph (2)(A) the court shall order the effective date of any approval of the drug or veterinary biological product 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.

Although the statute does not expressly reset the effective date when the 30-month stay expires before the patent is found to be infringed or a preliminary injunction granted, the statute, as informed by its legislative history, supports the district court's action of resetting the effective date. The House Report accompanying the Hatch-Waxman Act explains: "[I]n the case where an ANDA had been approved, the order would mandate a change in the effective date." H.R.Rep. No. 98-857, at 46 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2679.

Mylan argues that the district court's order is inconsistent with 21 U.S.C. § 355(j)(5)(B)(iii), which lays out two measures for delaying an ANDA's approval:

> 21 U.S.C. § 355(j)(5)(B)(iii)(II)(bb) provides: if the district court decides that the patent has been infringed before the expiration of the 30 month period, then the FDA's approval shall be made effective on the date specified by the district court in a court order under 35 U.S.C. § 271(e)(4)(A).
>
> 21 U.S.C. § 355(j)(5)(B)(iii)(IV) provides: if before the expiration of [the 30 month stay] the court grants a preliminary judgment ... and if the court decides that such patent has been infringed then the approval shall be made effective as in subclause (II).

[7] The district court, however, did not ignore these express conditions when resetting the effective date. Considering 35 U.S.C. § 271, the district court correctly discerned that the provisions quoted above do not limit the authority of the district court to reset the effective date in circumstances similar to those statutorily listed as indeed suggested by the legislative history for the provision. Indeed 21 U.S.C. § 355 does not limit a court's authority to reset for conditions other than those listed. This provision, directed at the FDA, instructs the agency regarding its responsibilities to process an ANDA. This provision does not limit the court's authority as noted. The district court was correct to reset the effective date of an ANDA directly under 35 U.S.C. § 271 without going through 21 U.S.C. § 355.

VII

In view of all the intrinsic and extrinsic evidence, the district court correctly construed claim 1 to cover Ortho-McNeil's epilepsy drug topiramate. Accordingly, this court affirms the district court's decision to permanently enjoin Mylan from infringing the '006 patent. This court also ***1367** affirms the dismissal of Mylan's invalidity defenses based on obviousness, inequitable conduct, and non-enablement and finds no error in the district court's decision to reset the effective date of Mylan's ANDA to a date not earlier than the date of expiration of the patent.

AFFIRMED

C.A.Fed. (N.J.),2008.
Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.
520 F.3d 1358, 86 U.S.P.Q.2d 1196

END OF DOCUMENT

865 F.2d 1247, 57 USLW 2436, 9 U.S.P.Q.2d 1461
(Cite as: 865 F.2d 1247)

United States Court of Appeals,
Federal Circuit.
UNITED STATES STEEL CORPORATION, Hercules, Inc., Shell Oil Company, Northern Petrochemical Company, Himont, U.S.A., Inc., Aristech Chemical Corporation, National Distillers and Chemical Corporation, and El Paso Products Company, Appellant,
v.
PHILLIPS PETROLEUM COMPANY, Appellee.

Nos. 88-1166 to 88-1171
Jan. 10, 1989.

Alleged infringers brought action challenging patent for crystalline polypropylene. The United States District Court for the District of Delaware, 673 F.Supp. 1278, Joseph J. Longobardi, J., found that patent was invalid and infringed, and alleged infringers appealed. The Court of Appeals, Markey, Chief Judge, held that: (1) invention of crystalline polypropylene was sufficiently disclosed in patentee's original 1953 application, so that filing date of original application rather than that of later application applied in determining whether patent was invalid as anticipated, and (2) principle of claimed invention was production for first time of crystalline polypropylene, and alleged infringers made no change at all on that principle, so that alleged infringers failed to establish any basis for restricting coverage of claim to less than its admitted literal scope under reverse doctrine of equivalents, and thus failed to establish that finding of infringement was clearly erroneous.

Affirmed.

West Headnotes

[1] Patents 291 90(1)

291 Patents
291III Persons Entitled to Patents
291k90 Original Inventors and Priority Between Inventors
291k90(1) k. In General. Most Cited Cases

Invention of crystalline polypropylene was sufficiently disclosed in patentee's original 1953 application, so that filing date of original application rather than that of later application applied in determining whether patent was invalid as anticipated. 35 U.S.C.A. § 112.

[2] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

Application for patent on crystalline polypropylene was not shown to be defective with regard to its description of utility or enablement. 35 U.S.C.A. §§ 101, 112.

[3] Patents 291 16.25

291 Patents
291II Patentability
291II(A) Invention; Obviousness
291k16.25 k. Chemical Compounds. Most Cited Cases

Alleged infringers failed to show that claimed invention of patent on crystalline polypropylene would have been obvious to one of ordinary skill in art, and thus did not show that patent was invalid for obviousness. 35 U.S.C.A. § 103.

[4] Patents 291 232

291 Patents
291XII Infringement
291XII(A) What Constitutes Infringement
291k228 Patents for Processes
291k232 k. Use of Process. Most Cited Cases

Principle of claimed invention of patent on crystalline polypropylene was production for first time of crystalline polypropylene, and alleged infringers made

no change at all on that principle, so that alleged infringers failed to establish any basis for restricting coverage of claim to less than its admitted literal scope under reverse doctrine of equivalents, and thus failed to establish that finding of infringement was clearly erroneous.

Patents 291 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original. Most Cited Cases

2,692,257, 3,112,300, 4,376,851. Cited.

Patents 291 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original. Most Cited Cases

4,376,851. Valid and Infringed.

***1248** Kenneth E. Madsen, Kenyon & Kenyon, New York City, and Stanton Lawrence, Pennie & Edmonds, New York City, argued for appellant. Francis T. Carr, Alan T. Bowes and James Galbraith, Kenyon & Kenyon, New York City, were on the brief, for appellant, of counsel. Also James A. Power, Jr., Pennie & Edmonds, of New York City, was on the brief, for appellant.

Harry J. Roper, Neuman, Williams, Anderson & Olson, Chicago, Ill., argued for appellee. With him on the brief, were Sidney Neuman, Nicholas A. Poulos and George S. Bosy, Chicago, Ill.

Before MARKEY, Chief Judge, NIES and MICHEL, Circuit Judges.

MARKEY, Chief Judge.

Consolidated appeals from a judgment of the United States District Court for the District of Delaware, *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F.Supp. 1278, 6 USPQ2d 1065 (D.Del.1987) (Longobardi J.), that defendants United States Steel Corporation and its successor in interest, Aristech Chemical Corporation; Hercules Inc.; Shell Oil Company; Northern Petrochemical Co. and its successor in interest, National Distillers and Chemical Corporation; Himont, U.S.A., Inc.; and El Paso Products Company (collectively defendants) had not proved United States Patent No. 4,376,851 ('851 patent) invalid or unenforceable, and that Phillips Petroleum Company (Phillips) had "met the burden required to prove that each of the consolidated defendants['] propylene homopolymer products infringe[s] the claim of the '851 patent." We affirm the district court in all respects.

BACKGROUND

The basic concepts of polymer chemistry, the history of polypropylene, and the interference and court proceedings leading to Phillips' '851 patent are exhaustively explored and explicated in Judge Longobardi's full-service opinion. *See Phillips Petroleum*, 673 F.Supp. at 1278, 6 USPQ2d at 1065; *see also Standard Oil Co. v. Montedison S.p.A.*, 494 F.Supp. 370, 207 USPQ 298 (D.Del.1980) (Wright, J.), *aff'd*, 664 F.2d 356, 212 USPQ 327 (3d Cir.1981), *cert. denied*, 456 U.S. 915, 102 S.Ct. 1769, 72 L.Ed.2d 174 (1982). Familiarity with those opinions being assumed, we discuss only the dispositive facts in conjunction with ***1249** defendants' arguments to which they relate.

The Claim

The sole claim of the '851 patent, which had been the count of the interference, reads:

> Normally solid polypropylene, consisting essentially of recurring propylene units, having a substantial crystalline polypropylene content.[FN1]
>
> FN1. All parties agree that the "crystalline" content of the polypropylene claimed in the '851 patent occurs because all the pendent methyl groups (CH_3) are oriented in a regular pattern on the "same side" of the polymer backbone (*i.e.*, in an "isotactic" arrangement).
>
> For more extensive discussion of the technology, see 673 F.Supp. at 1284-86, 6 USPQ2d at 1067-68; 494 F.Supp. at 376-78, 206 USPQ at 687-89.

The '851 patent issued on an application filed in 1956 as a continuation-in-part of application Serial No. 333,576 filed by Hogan and Banks on January 27, 1953 (the 1953 application) and of application Ser. No. 476,306 also filed by Hogan and Banks on December 20, 1954 (the 1954 application).[FN2]

FN2. Because the 1953 and 1954 applications and specifications are virtually identical, we discuss only the former.

Defendants' Presentation of the Appeal

I. In attacking the holding that they had not proved the '851 patent invalid, defendants state several grounds for invalidity: (1) anticipation by U.S. Patent No. 3,112,300 (the '300 patent) to Montecatini (an Italian Corporation) as assignee of Guilio Natta et al.; (2) inadequate disclosure of specific utility under 35 U.S.C. §§ 101 and 112; (3) obviousness in light of Patent No. 2,692,257 ('257 patent) to Standard Oil Company (Indiana) as assignee of Alex Zletz; (4) double patenting (same-invention and obviousness types).

II. Defendants attack the finding of infringement on grounds that the district court erred in: (1) concluding that defendants admitted literal infringement; (2) construing the prosecution history, determining the scope of the claim, and treating interference estoppel; and (3) considering the reverse doctrine of equivalents.

III. Defendants say the district court erred in not finding Phillips guilty of inequitable conduct in the PTO.

OPINION

I. *Validity*

(1) Anticipation

It is undisputed that the '300 patent [FN3] would anticipate the '851 patent if Phillips were not entitled to rely on the filing date of the 1953 application. *See* 35 U.S.C. § 120 (1982).[FN4] Defendants argue that Phillips is not so entitled because the 1953 specification neither describes nor enables (35 U.S.C. § 112) what they call the "broad" claim of the '851 patent.

FN3. The '300 patent describes the preparation of crystalline polypropylene using catalysts developed by Professor Karl Ziegler. Ziegler and Natta were awarded Nobel prizes for their discoveries.

FN4. Section 120 reads:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, ... by the same inventor shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

(a) *The 1953 Specification*

The 1953 specification says the invention relates to the polymerization of olefins and that one "aspect of the invention is concerned with the production of novel tacky and solid polymers." That specification was before our predecessor court in *In re Hogan*, 559 F.2d 595, 598, 194 USPQ 527, 530 (CCPA 1977), where the court said the "application discloses solid polymers made from 1-olefin monomers having a maximum chainlength of eight carbon atoms and no branching nearer the double bond ***1250** than the 4-position." The specification discloses that polymerization of propylene in the presence of a chromium oxide catalyst yields a solid polymer having a melting point in the range of 240 to 300° F, density in the range of 0.90 to 0.95, an intrinsic viscosity in the range of 0.2 to 1.0, and a weight *average* molecular weight range of approximately 5,000 to 20,000. The specification also discloses that the polypropylene compounds produced had *individual* molecular weights ranging from about 200 to about 50,000.

(b) *District Court Opinion*

The district court concluded that Phillips could rely on the filing date of the 1953 application (removing the '300 patent as prior art) because "[t]he properties described [in the 1953 specification] would indicate to one skilled in the art that Phillips was in possession of a new, crystalline form of propylene," 673 F.2d at 1290, 6 USPQ2d at 1072, and because undisputed evidence "demonstrated that [the specifi-

cation] enable[d] the production of [the] polypropylene of the '851 claim." *Id.* at 1292, 6 USPQ2d at 1073.

In the district court's view, defendants' arguments and evidence missed the point:

> [W]ith respect to both the written description and enablement requirements, [d]efendants have misconstrued the inquiry under section 112. They have sought to read into the '851 claim a molecular weight/intrinsic viscosity limitation which simply is not there. Nearly thirty-five years after Phillips' application was filed, they fault Phillips for not describing a polypropylene of high molecular weight/intrinsic viscosity, a property which we *now* know to be extremely important. A patent applicant is not required, however, to predict every possible variation, improvement[,] or commercial embodiment of his invention.

Id. at 1292, 6 USPQ2d at 1074 (citations & footnote omitted) (emphasis in original). Further evaluating the evidence, the district court noted that the "great deal of [defendants'] evidence designed to demonstrate the differences in physical and mechanical properties of their commercial polypropylenes, on the one hand, and polypropylene having an intrinsic viscosity within the range specified in the 1953 application," was such that it "in no way aids [d]efendants in their attempt to establish the inadequacy of Phillips' 1953 application." *Id.* at 1290 n. 5, 6 USPQ2d at 1072 n. 5. [FN5]

> FN5. That evidence included showing that the accused polypropylenes had higher intrinsic viscosities and average molecular weights than the corresponding properties set forth in the 1953 specification, and evidence tending to indicate, in defendants' view, that "the propylene of the 1953 application is weak and brittle" and "essentially useless as a plastic," whereas the accused polypropylenes are "tough materials, resistant to stress" having "plastic properties."

(c) *Defendants' Arguments on Anticipation*

[1] Defendants do not dispute that: (1) the properties reported in the 1953 specification indicate that the polypropylene has substantial crystallinity; (2) the 1953 specification described crystalline polypropylene; (3) Hogan and Banks were the first to polymerize crystalline polypropylene; (4) polypropylene prepared by Hogan and Banks before the 1953 filing date contained the same crystalline isotactic structure exhibited by the Natta polypropylene made with a Ziegler catalyst; and (5) the 1953 specification enabled one skilled in the art to practice the claimed invention, *i.e.*, to make recurring units of polypropylenes "having a substantial crystalline polypropylene content."

Challenging no finding of the district court, defendants argue that the court misstated the law. Per defendants, "[t]he question is not what the claim 'sets forth,' but what it embraces. If it embraces subject matter for which no adequate basis exists in the underlying disclosure, the claim is too broad." Pointing to differences in intrinsic viscosity and average molecular weight, defendants argue that the 1953 disclosure does not "reasonably convey [ ] to the artisan that the inventor had *possession at the time* [1953] *of all of the later-claimed subject matter,*" and that "the scope of enablement provided to that artisan by the prior application was [not] ***1251** reasonably commensurate with the full scope of protection sought by the *later claim.*" (Emphasis defendants'). Stripped to its basics, defendants' argument is one of "overbreadth", but that word alone has long ago been discredited as a basis for determining sufficiency of a specification. *See In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369, 58 CCPA 1069 (1971) (Patent Office should be concerned with support or non-support of a generic term, not its breadth); *In re Hogan*, 559 F.2d 595, 605-06, 194 USPQ 527, 537 (CCPA 1977) ("Rejections under § 112, first paragraph, on the ground that the scope of enablement is not commensurate with the scope of the claims, orbit about the more fundamental question: To what scope of protection is the applicant's particular contribution to the art entitled?").

It is true that adequacy of support is judged in relation to the scope of the claims, *see In re Moore*, 439 F.2d 1232, 1236, 169 USPQ 236, 239, 58 CCPA 1042 (1971); *In re Borkowski*, 422 F.2d 904, 909, 164 USPQ 642, 646, 57 CCPA 946 (1970), but defendants fail to recognize that "application sufficiency under § 112, first paragraph, must be judged as of the filing date." *In re Glass*, 492 F.2d 1228, 1232, 181 USPQ 31, 34 (CCPA 1974); *see In re Hogan*, 559 F.2d at 604, 194 USPQ at 535 (§ 112's enablement requirement); *In re Koller*, 613 F.2d 819, 823, 204 USPQ 702, 706 (CCPA 1977) (§ 122's written description require-

ment). In the context of section 120, in this case, focusing on the filing date requires that the claim of the '851 patent be treated as though it were filed in 1953. Only if that claim would at that time have been correctly rejected for lack of support in the 1953 specification may the patentee be denied use of section 120 to predate the intervening reference to the '300 patent. *See In re Hogan*, 559 F.2d at 604, 194 USPQ at 537.

In re Koller is particularly illustrative. The claims there at issue and claims contained in a grandparent application contained the broad term "liquid medium." The PTO board held that appellants could not rely on the grandparent's filing date because "[t]he broad recitation 'liquid medium' would have been construed by one skilled in the art from the disclosure as consisting of water or water to which a miscible organic solvent is added." 613 F.2d at 822, 204 USPQ at 705. Because of a later discovery that water-immiscible solvents could be used, the board emphasized that "[t]he term [liquid medium] as now interpreted by appellants is broader than that disclosed in the grandparent application." *Id.* The board concluded:

> The fact that the recitation "liquid medium" might include water-immiscible solvents is not sufficient indication to one of ordinary skill at that time that such medium was part of appellants' invention. On the contrary, a fair reading of the grandparent disclosure would have led one to conclude that the isomerization in water and water-miscible media was appellants' contribution. Accordingly, it is our view that appellants are not entitled to the benefit of their grandparent application....

Id. at 823, 204 USPQ at 705 (citation omitted).

Our predecessor court reversed, citing the general rule that "language in a specification is to be understood for what it meant to one having ordinary skill in the art at the time the application was filed," *id.* at 824, 204 USPQ at 706, and noting that support need be found for only the claimed invention, in view of how one skilled in the art at that time would construe the claims and would read its specification. *Id.*; *see Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed.Cir.1985).

Defendants' misdirected approach here is the same as that improperly relied upon by the PTO in *Hogan.* Defendants do not, as they cannot, argue that the 1953 specification fails to enable one skilled in the art to practice the *claimed invention.* That the '851 claim may cover a later version of the claimed composition (crystalline polyproplene with higher intrinsic viscosity and average molecular weight) relates to infringement, not to patentability. *See* ***1252***In re Hogan*, 559 F.2d at 607, 194 USPQ at 538.[FN6] To hold differently would, in the words of *Hogan*, "impose an impossible burden on inventors and thus on the patent system." 559 F.2d at 606, 194 USPQ at 537.

> FN6. Defendants' attention is particularly directed to the discussion of *In re Ranier*, 390 F.2d 771, 156 USPQ 334, 55 CCPA 853 (1968), and *In re Fisher*, 427 F.2d 833, 166 USPQ 18, 57 CCPA 1099 (1970), found in *Hogan.* In *Hogan* the court noted that statements in *In re Moore*, that " 'the scope of enablement' must be 'commensurate with the scope of protection sought,' impel[led] clarification." 559 F.2d at 605, 194 USPQ at 536.

In sum, in determining sufficiency of support it is the state of the art in 1953 and level of skill in the art at that time that is critical. *Id.* at 605, 194 USPQ at 537 ("i.e., of the condition of knowledge about all art-related facts existing in 1953").

Thus the district court correctly held defendants' evidence immaterial to the section 112, first paragraph inquiry. The central flaw in defendants' evidence, as recognized by the district court, is that it was directed solely to a later state of the art. The record evidences that until 1954, when Natta used the Ziegler catalyst, no one thought it possible that propylene monomers could be polymerized into polyproplene with an intrinsic viscosity of 1.7 to 2.0 and an *average* molecular weight approaching 50,000. Similarly insufficient is defendants' evidence that the art since 1930 recognized the desirability of high molecular weight polymers. Hogan and Banks disclosed polypropylene with far better properties, including an average molecular weight up to 20,000, than were known in the art in 1953. Moreover, evidence of record establishes that crystallinity gives polypropylene the properties of tensile strength, stiffness, and hardness, and, as above indicated, defendants concede that Hogan and Banks were the first to teach crystallinity.

Simply put, defendants' reliance on the 1953 specification's listing of the properties of the polypropylene produced and there disclosed is bootless. As stated in *In re Koller:* "[c]ertainly, the disclosure of specifics *adds* to the understanding one skilled in the art would glean from a generic term, but it does not follow that such added disclosure *limits* the meaning thereof." 613 F.2d at 823, 204 USPQ at 705 (emphasis in original).[FN7]

FN7. It is of no moment in this case that the 1953 specification differs from the '851 patent specification. The former provides support for the claimed invention and the latter does not undermine that support.

(2) Specific Utility

[2] Contrary to Defendants' arguments, the district court did not err in determining that defendants failed to meet their burden of showing "that the 1953 application is defective under [35 U.S.C. §§] 101 and 112." 673 F.Supp. at 1333, 6 USPQ at 1108.[FN8]

FN8. "We review utility [§ 101] as a question of fact and enablement [§ 112] as a question of law." *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1268, 229 USPQ 805, 810 (Fed.Cir.1986), *cert. denied,* 479 U.S. 1030, 107 S.Ct. 875, 93 L.Ed.2d 829 (1987).

The court's section 101 finding must be affirmed because we affirm, *infra,* the court's infringement finding. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 959, 220 USPQ 592, 598 (Fed.Cir.1983) ("correct finding of infringement of otherwise valid claims mandates as a matter of law a finding of utility under § 101"), *cert. denied,* 469 U.S. 835, 105 S.Ct. 127, 83 L.Ed.2d 69 (1984).

We affirm the court's conclusion that defendants had not proven the 1953 specification's description of utility defective under section 112. That defendants' arguments are baseless is immediately apparent upon reading Judge Longobardi's rejection of those arguments. *See* 673 F.Supp. at 1325-33, 6 USPQ2d at 1101-08.

(3) Obviousness

[3] The district court did not err in determining that defendants had not, by clear and convincing proof, established facts requiring a conclusion that the claimed invention would have been obvious to one of ordinary skill in the art. *See* 35 U.S.C. § 103 (1982). Defendants are unpersuasive in arguing that the court erred in construing***1253** the '257 patent's disclosure. Nor do defendants show to have been clearly erroneous the finding that Mr. Peters deviated from the '257 patent's teaching in experiments P-1 and P-9. *See Anderson v. City of Bessemer City, N.C.*, 470 U.S. 564, 573-74, 105 S.Ct. 1504, 1511-12, 84 L.Ed.2d 518 (1984); Fed.R.Civ.P. 52(a).

In sum, we find no error in the district court's assessment of the content of the prior art or its assessment of the differences between that art and the claimed invention.

Conclusion on Validity

Defendants have shown no error in the district court's determination that they failed to carry their burden of proof on the issue of validity. 35 U.S.C. § 282 (1982).

II. *Infringement-Reverse Doctrine of Equivalents*

[4] Having found that the defendants' polypropylene literally infringed the '851 claim, the district court went on to reject defendants' arguments directed to the reverse doctrine of equivalents.[FN9] Saying the district court misconstrued that doctrine, defendants, as they did at trial, compare their product with only that disclosed in the 1953 application. Defendants' comparison fails, first, because, as they concede, the 1953 specification disclosed polypropylene having substantial crystallinity. Second, as correctly noted by the district court, the claim of the '851 patent issued on Phillips' 1956 application. We agree with the district court that the principle of the claimed invention, as corroborated by the work of Hogan and Banks between 1951 and 1953 and the 1953 application, "is the production for the first time of crystalline polypropylene." 673 F.Supp. at 1354, 6 USPQ2d at 1126, and that defendants made no change at all in that principle.

FN9. The reverse doctrine of equivalents can in some cases be seen as conceptually and linguistically difficult to apply when the claim is drawn to chemical compounds or compositions. The doctrine speaks of performance of a "function" in a substantially different "way." The district court here did not face that difficulty, having focused on the "principle" of the contribution made by the

inventor and found it unchanged in the accused product.

Defendants supply no legal basis or equitable ground, and we see none, for restricting the coverage of the claim to less than its admitted literal scope.[FN10] We are unpersuaded of error of any kind in the district court's consideration of the "principle" of the claimed invention, *see* *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608-09, 70 S.Ct. 854, 856, 94 L.Ed. 1097 (1950)) and its rejection of defendants' argument based on a misdirected comparison. In sum, defendants have not shown that the district court's finding of infringement was clearly erroneous.[FN11]

FN10. We especially note that the claim of the '851 patent was the count of a thirteen-year, five-party interference set up to determine priority in relation to what the defendant's classify as the invention of "high molecular weight" polypropylene.

FN11. That the product claimed in the '300 patent may be patentable does not mean that a person making, using, or selling that product cannot be guilty of infringing the '851 patent. "Dominating" patents are not uncommon. *See* *In re Kaplan*, 789 F.2d 1574, 1577, 229 USPQ 678, 681 (Fed.Cir.1986).

III. *Remaining Arguments*

We have carefully considered defendants' arguments regarding: (1) double patenting (including the construction of claim 16 of U.S. Patent No. 2,825,721); (2) literal infringement (based on asserted errors in construction of the prosecution history, determination of claim scope, and treatment of interference estoppel); and (3) inequitable conduct. We find none persuasive of error in the district court's disposition of any of those issues and none of sufficient import to require discussion here of that disposition.[FN12]

FN12. Because the district court made a separate, independent finding of literal infringement, a finding not shown to have been clearly erroneous, we need not and do not discuss defendants' argument on whether they "admitted" literal infringement.

***1254** IV. *Conclusion*

The judgment of the district court is affirmed in all respects.

AFFIRMED.

C.A.Fed. (Del.),1989.
U.S. Steel Corp. v. Phillips Petroleum Co.
865 F.2d 1247, 57 USLW 2436, 9 U.S.P.Q.2d 1461

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413 F.3d 1318, 75 U.S.P.Q.2d 1297
(Cite as: 413 F.3d 1318)

United States Court of Appeals,
Federal Circuit.
Gary H. RASMUSSON and Glenn F. Reynolds, Appellants,
v.
SMITHKLINE BEECHAM CORPORATION, Cross-Appellant.

Nos. 04-1191, 04-1192.
June 27, 2005.

Background: In an interference proceeding, the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office (PTO) issued an order redeclaring interference with patents for a method of treating prostate cancer by using finasteride as a selective inhibitor, and applicant appealed.

Holdings: The Court of Appeals, Bryson, Circuit Judge, held that:
(1) applicant was not entitled to a priority date for application earlier than the priority date of assignee's patents and the corresponding reissue applications, and
(2) foreign application was enabled for purposes of anticipation.

Affirmed in part, reversed in part, and remanded.

West Headnotes

[1] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

"How to use" prong of enablement requirement incorporates the requirement that the patent specification disclose as a matter of fact a practical utility for the invention. 35 U.S.C.A. §§ 101, 112.

[2] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

Patent applicant's failure to disclose how to use an invention may support a rejection either for lack of enablement, as a result of the specification's failure to disclose adequately to one ordinarily skilled in the art how to use the invention without undue experimentation, or for lack of utility when there is a complete absence of data supporting the statements which set forth the desired results of the claimed invention. 35 U.S.C.A. §§ 101, 112.

[3] Patents 291 49

291 Patents
291II Patentability
291II(C) Utility
291k49 k. Evidence of Utility. Most Cited Cases

In the context of determining whether sufficient utility as a drug, medicant, and the like in human therapy has been alleged, it is proper for patent examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the allegations as obviously correct. 35 U.S.C.A. §§ 101, 112.

[4] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

Where there is no indication that one skilled in the art would accept without question statements as to the effects of the claimed drug products and no evidence has been presented to demonstrate that the claimed products do have those effects, patent applicant has failed to demonstrate sufficient utility and therefore cannot establish enablement. 35 U.S.C.A. §§ 101, 112.

[5] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

All applications prior to applicant's ninth application for patent for a method of treating prostate cancer by using finasteride as a selective inhibitor were not enabled, and therefore applicant was not entitled to a priority date earlier than the priority date of assignee's patents and the corresponding reissue applications; applicant was unable to show, prior to his ninth application, that a person of ordinary skill in the art would not have believed that finasteride was effective in treating prostate cancer. 35 U.S.C.A. § 112.

[6] Patents 291 65

291 Patents
291II Patentability
291II(D) Anticipation
291k63 Prior Patents
291k65 k. Sufficiency of Description. Most Cited Cases

A patent claim cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled. 35 U.S.C.A. § 112.

[7] Patents 291 65

291 Patents
291II Patentability
291II(D) Anticipation
291k63 Prior Patents
291k65 k. Sufficiency of Description. Most Cited Cases

Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of Invention in Specification. Most Cited Cases

Standard for what constitutes proper enablement of a prior art reference for purposes of anticipation differs from enablement standard pertaining to requirement that specification must enable one skilled in the art to use the invention. 35 U.S.C.A. §§ 102, 112.

[8] Patents 291 65

291 Patents
291II Patentability
291II(D) Anticipation
291k63 Prior Patents
291k65 k. Sufficiency of Description. Most Cited Cases

Prior art reference need not demonstrate utility in order to serve as an anticipating reference. 35 U.S.C.A. § 102.

[9] Patents 291 65

291 Patents
291II Patentability
291II(D) Anticipation
291k63 Prior Patents
291k65 k. Sufficiency of Description. Most Cited Cases

Proof of efficacy is not required in order for a reference in patent application to be enabled for purposes of anticipation. 35 U.S.C.A. § 102.

[10] Patents 291 69

291 Patents
291II Patentability
291II(D) Anticipation
291k67 Prior Description in Printed Publication
291k69 k. Sufficiency of Description. Most Cited Cases

Findings that there was no reasonable scientific basis for a person of ordinary skill in the art to conclude that the claimed method for treating prostate cancer by using finasteride as a selective inhibitor would be effective in treating prostate cancer, and that, given the lack of proof provided in the publication itself, a person of ordinary skill in the art as of the publication date of foreign patent application would

not have believed that the method described in application would be effective were insufficient to support conclusion that foreign application was not an enabling reference for purposes of anticipation. 35 U.S.C.A. § 102 .

Patents 291 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original Utility. Most Cited Cases

5,496,556, 5,637,310. Cited.

***1320** Robert L. Baechtold, Fitzpatrick, Cella, Harper & Scinto, of New York, New York, argued for appellants. With him on the brief were Daniel S. Glueck and Stephen E. Belisle, of Washington, DC.

Herbert H. Mintz, Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., of Washington, DC, argued for cross appellant. With him on the brief was Lara C. Kelley.

Before BRYSON, Circuit Judge, PLAGER, Senior Circuit Judge, and PROST, Circuit Judge.

BRYSON, Circuit Judge.

This is an appeal from an interference proceeding before the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office ("PTO"). At issue in the interference proceeding were a set of claims from U.S. Patent Application Serial No. 08/460,296 ("the '296 application"), and another set of claims from U.S. Patent Nos. 5,637,310 ("the '310 patent") and 5,496,556 ("the '556 patent") and their corresponding reissue applications, U.S. Patent Application Serial Nos. 09/964,383 ("the '310 reissue patent application") and 09/984,083 ("the '556 reissue patent application"). Gary H. Rasmusson and Glenn F. Reynolds (collectively, "Rasmusson") are the inventors named on the '296 application. SmithKline Beecham Corporation is the assignee of the '310 and '556 patents and the corresponding reissue patent applications. The Board of Patent Appeals and Interferences held that Rasmusson was not entitled to the benefit of a priority date based on certain previous applications and that Rasmusson could not defeat the priority date accorded to SmithKline's patents and reissue applications. Because that decision is supported by substantial evidence and is not contrary to law, we affirm. The Board also held that SmithKline's patents and reissue patent applications were not anticipated by a European patent application, EP No. 285383 ("EP '383"). The Board based that ruling on its conclusion that EP '383 was not enabled. We reverse that aspect of the Board's decision and find that EP '383 was enabled for purposes of anticipation. We therefore remand this case to the Board for a determination of the effect of that application on the claims of SmithKline's patents and reissue patent applications and Rasmusson's '296 application.

I

A

This case relates to a method of treating a type of prostate cancer by administering a chemical compound called finasteride. Finasteride inhibits the production of an enzyme known as 5-<<alpha>>-reductase ("5<<alpha>>R"), which is responsible for converting the hormone testosterone to dihydrotestosterone ("DHT"). Both testosterone and DHT are in the class of hormones known as androgens, which bind to receptors on certain target cells and initiate a chain of biological events that are important in the expression of male sex characteristics. DHT is known to be a more potent androgen than testosterone, and high levels of DHT are associated with prostate cancer. As a result, numerous attempts have been made to decrease DHT levels by seeking out inhibitors of the 5<<alpha>>R enzyme.

There are two main categories of 5<<alpha>>R inhibitors: "selective" (or "pure") and "multi-active." Multi-active inhibitors not only inhibit the 5 R enzyme, but also reduce***1321** the effects of testosterone by competing with testosterone for the same target receptor sites. Selective 5<<alpha>> inhibitors decrease the level of DHT solely by inhibiting the production of the 5 R enzyme, thereby eliminating any side effects associated with blocking testosterone. The parties agree that finasteride acts as a selective 5<<alpha>>R inhibitor.

B

Rasmusson's '296 application was filed on June 2, 1995. It is the ninth in a series of applications stemming from U.S. Patent Application No. 07/034,808,

which was filed on April 3, 1987. The '296 application is directed to "Methods of treating Prostatic Carcinoma with 17-Beta-N-mon osubstituted-carbamoyl-4-aza-5<<alpha>>-androst-1-en-3-ones." SmithKline's '310 and '556 patents and the corresponding reissue applications were previously accorded the benefit of a filing date of another issued patent, U.S. Patent No. 5,300,294 ("the '294 patent"). That filing date is June 27, 1990. Those patents and their corresponding reissue applications cover a "Method of Treating Prostatic Adenocarcinoma by employing a steroid 5-<<alpha>>-reductase inhibiting compound or a combination of steroid 5- -reductase inhibiting compounds."

On January 22, 2001, the PTO declared an interference between the claims of Rasmusson's '296 application and SmithKline's '310, '556, and '294 patents, although the Board later dismissed the '294 patent from the interference. Before the Board, Rasmusson moved to have SmithKline's claims rejected, and SmithKline moved to deny Rasmusson the benefit of its eight earlier applications and to add claims to the interference from the reissue patent applications corresponding to the '310 and '556 patents.

After considering preliminary motions from both sides, the Board granted SmithKline's motion to deny Rasmusson the benefit of its eight earlier applications and to add the '310 and '556 reissue patent applications to the interference. The Board also granted Rasmusson's motion to hold the relevant claims from SmithKline's '310 and '556 patents invalid, but denied Rasmusson's motion to hold the claims of the '310 and '556 reissue patent applications invalid based on anticipation by the European counterpart to Rasmusson's first application.

As a result of its rulings on invalidity, the Board issued an Order Redeclaring Interference, which substituted a new count for the count previously declared in the interference.[FN1] The replacement count reads as follows:

> FN1. The replacement count corresponds to claims 1-8 of the '296 patent, claim 1 of the '310 patent, claim 1 of the '556 patent, claims 1 and 3 of '310 reissue patent application, and claims 1 and 2 of the '556 reissue patent application. Because the Board held claim 1 of the '310 and claim 1 of the '556 patents to be invalid, and because claim 1 of the '310 reissue application and claim 1 of the '556 reissue application were based on those invalidated claims, the only SmithKline claims incorporated in the replacement count were claim 3 of the '310 reissue application and claim 2 of the '556 reissue application.

> The method of claim 4 of the Rasmusson 08/460,296 application wherein the animal is human[;] or [t]he method of claim 3 of the [SmithKline] 09/964,383 application[;] or [t]he method of claim 2 of the [SmithKline] 09/984,083 application. Claim 4 of Rasmusson's '296 application depends on claim 3, which, in turn, depends on claim 1. Taking the language of all three claims into account, the Board summarized claim 4 as follows:
>
> A method of treating prostatic carcinoma in animals including humans which comprises administering a therapeutically effective amount of the compound
> ***1322**
> 17<<beta>>-(N-tertbutylcarbamoyl)-4-aza-5<<alpha>>-androst-1-en-3-one.
>
> The chemical compound recited in claim 4 is a formula for finasteride.

Claim 3 of SmithKline's '383 application reads as follows:

> A method of treating human prostatic adenocarcinoma which comprises administering to a subject in need thereof an oral dosage unit containing about 1 mg. to about 500 mg. of a steroid 5-<<alpha>>-reductase inhibiting compound from 1-6 times during a twenty four hour period.

Claim 2 of SmithKline's '083 application reads as follows:

> A method of treating human prostatic adenocarcinoma which comprises administering in a human subject in need thereof, a dosage unit containing about 0.1 mg/kg to about 100 mg/kg of 17<<beta>>-(N-tertbutylcar boxamide)-5-<<alpha>>-androst-1-ene-4-aza-3-one from one to six times daily.

The chemical formula recited in claim 2 is a

representation of finasteride.

After the Board issued its decision on the parties' preliminary motions and its Order Redeclaring Interference, Rasmusson requested reconsideration of the Board's motion decision. The Board reaffirmed its earlier decision. Rasmusson appeals from aspects of the Board's ruling; SmithKline has filed a conditional cross-appeal.

II

The June 27, 1990, filing date accorded to SmithKline's patents and reissue applications falls between the filing dates of Rasmusson's third and fourth applications. In order to overcome the June 27, 1990, filing date, Rasmusson therefore sought priority on the basis of his first, second, and third applications, which were filed on April 3, 1987; May 19, 1988; and June 21, 1989, respectively. The Board found that Rasmusson was not entitled to priority based on any of those filing dates because the corresponding applications failed to satisfy the written description and enablement requirements of 35 U.S.C. § 112.

With respect to enablement, the Board found that none of the applications filed before the ninth application "would have enabled a person of ordinary skill in the art as of each of the respective filing date[s] to treat human prostate cancer by administering a therapeutically effective amount of finasteride to a human in need thereof without undue experimentation." The Board based that finding on its determination that a person of ordinary skill in the art would have had no basis as of the filing date of the eighth application for believing that finasteride could be used to treat prostate cancer in light of the state of the art and in light of Rasmusson's failure to provide any data to demonstrate the effects of finasteride in treating prostate cancer.

On appeal, Rasmusson asserts that the specifications of the respective applications are enabling because a person of ordinary skill in the art could perform the steps of the disclosed method without the need for any experimentation. Rasmusson argues that the Board's finding regarding efficacy does not support its finding of lack of enablement. According to Rasmusson, efficacy is not relevant to enablement, but pertains only to the issue of utility under 35 U.S.C. § 101. Because the Board did not make a determination based on section 101, Rasmusson asserts that the Board erred.

[1][2] We disagree. In order to satisfy the enablement requirement of section 112, an applicant must describe the manner of making and using the invention "in such full, clear, concise, and exact terms as to enable any person skilled in the art ... to make and use the same ...." 35 U.S.C. § 112, para. 1. As this court has explained, ***1323** "the how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention." *In re Cortright*, 165 F.3d 1353, 1356 (Fed.Cir.1999), *quoting In re Ziegler*, 992 F.2d 1197, 1200 (Fed.Cir.1993); *see also In re Schoenwald*, 964 F.2d 1122, 1124 (Fed.Cir.1992) (stating that utility must be disclosed to satisfy the section 112 enablement requirement). In explaining what constitutes a sufficient showing of utility in the context of the enablement requirement, this court has stated that an applicant's failure to disclose how to use an invention may support a rejection under either section 112, paragraph 1 for lack of enablement, or "section 101 for lack of utility 'when there is a complete absence of data supporting the statements which set forth the desired results of the claimed invention.' " *Cortright*, 165 F.3d at 1356, *quoting Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762 (Fed.Cir.1984).

[3][4] In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, "it is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the allegations as obviously correct." *In re Jolles*, 628 F.2d 1322, 1325 (Cust. & Pat.App.1980), *citing In re Novak*, 49 C.C.P.A. 1283, 306 F.2d 924 (Cust. & Pat.App.1962); *see Application of Irons*, 52 C.C.P.A. 938, 340 F.2d 974, 977-78 (Cust. & Pat.App.1965). Indeed, in *In re Brana*, 51 F.3d 1560 (Fed.Cir.1995), we stated that "a specification disclosure which contains a teaching of the manner and process of making and using the invention ... must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *Id.* at 1566, *quoting Marzocchi*, 58 C.C.P.A. 1069, 439 F.2d 220, 223 (Cust. & Pat.App.1971); *Fiers v. Revel*, 984 F.2d 1164, 1171-72 (Fed.Cir.1993), *quoting Marzocchi*, 439 F.2d at 223; *see also Application of Armbruster*, 512 F.2d

676, 677 (Cust. & Pat.App.1975); *Application of Knowlton*, 500 F.2d 566, 571 (Cust. & Pat.App.1974); *Application of Bowen*, 492 F.2d 859 (Cust. & Pat.App.1974); *Application of Hawkins*, 486 F.2d 569, 576 (Cust. & Pat.App.1973). However, where there is "no indication that one skilled in [the] art would accept without question statements [as to the effects of the claimed drug products] and no evidence has been presented to demonstrate that the claimed products do have those effects," an applicant has failed to demonstrate sufficient utility and therefore cannot establish enablement. *Novak*, 306 F.2d at 928.

[5] In the applications at issue in this case, Rasmusson claimed a method of treating prostate cancer by using finasteride as a selective 5<<alpha>>R inhibitor. While both parties agree that a person of ordinary skill in the art at the time of Rasmusson's applications would have recognized that finasteride was a selective 5<<alpha>>R inhibitor, the parties disagree as to whether a person of ordinary skill in the art would have believed, before June 27, 1990, that finasteride would be effective in treating prostate cancer. Relying on articles demonstrating that various multi-active 5<<alpha>>R inhibitors were effective in treating prostate cancer, Rasmusson argues that a person of ordinary skill in the art at the time of his applications would have believed that administering a therapeutically effective amount of finasteride could be used for treating human prostate cancer. For that reason, Rasmusson asserts that he did not need to provide any data to demonstrate the efficacy of finasteride.

***1324** The Board found that a person of ordinary skill in the art would not have believed that finasteride was effective in treating prostate cancer simply because finasteride was known to be a selective 5<<alpha>>R inhibitor. That finding is supported by substantial evidence. Based on scientific articles and expert testimony from both parties, the Board found that a person of ordinary skill in the art as of August 10, 1993, the filing date of the eighth application, would not have concluded that a selective 5<<alpha>>R inhibitor would have any anti-tumor effects, because the anti-tumor effects shown by published experiments involving multi-active 5<<alpha>>R inhibitors could be attributable to contaminating activities having no relation to 5<<alpha>>R inhibition. In particular, the Board referred to articles and testimony to show that a person of ordinary skill in the art as of the filing date of the eighth application would not know that 5<<alpha>>R inhibition contributed to any anti-tumor effects, because it was not clear whether DHT or testosterone caused prostate cancer. If testosterone, and not DHT, caused the disease, then the anti-tumor effects resulting from multi-active 5<<alpha>>R inhibitors were not due to 5<<alpha>>R inhibition, but rather to anti-testosterone mechanisms such as the inhibition of testosterone receptor binding.

The Board referred to evidence pertinent to each of the relevant Rasmusson application filing dates, from the mid-1980s to the mid-1990s. In particular, the Board referred to a 1991 article by Dr. Glenn Gormley stating that "the concept that androgen-dependent prostate cancer is exclusively dependent on DHT and not testosterone has yet to be definitively established." Likewise, the Board referred to a 1992 article by Dr. Joseph Presti stating that "[w]hether prostatic cancer cells are dependent upon [DHT] rather than testosterone is not well defined." The Board concluded, however, that as of the filing date of the ninth application, June 2, 1995, a person of ordinary skill in the art would have believed that 5 R inhibition could play a role in treating prostate cancer in light of a presentation made by Dr. Ruben Gittes at the American Urological Association in August 1994, in which he reported successful results from treating prostate cancer with finasteride. Therefore, the Board determined that Rasmusson could claim priority as of the filing date of his most recent continuation application, which is June 2, 1995. While Rasmusson submitted articles supporting the use of multi-active inhibitors for treating prostate cancer, the Board found that those articles were not sufficient, because Rasmusson was claiming that the efficacy of finasteride was based on 5 R inhibition, as opposed to other effects.

Rasmusson did not make any contrary showing that a person of ordinary skill in the art as of the filing date of the third application would have recognized that a selective 5<<alpha>>R inhibitor in general, or finasteride in particular, would be effective in treating prostate cancer. In particular, the evidence cited by Rasmusson on appeal does not contravene the Board's finding, because that evidence is either dated too late with respect to the respective filing dates of the applications or pertains only to the use of multi-active inhibitors to treat prostate cancer. In order to obtain a

priority date earlier than June 27, 1990, Rasmusson needed to provide experimental proof that his invention could be effective in treating cancer. Because Rasmusson failed to do so and obtained a priority date only as of the filing date of his '296 application, the Board was correct to find that all applications prior to that application were not enabled, and that Rasmusson is not entitled to a priority date earlier than the priority date of SmithKline's '310 and '553 patents and the corresponding reissue applications.

***1325** Rasmusson argues that the enablement requirement of section 112 does not mandate a showing of utility or, if it does, it mandates only a showing that it is "not implausible" that the invention will work for its intended purpose. As we have explained, we have required a greater measure of proof, and for good reason. If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis. Because we have upheld the Board's determination of priority due to lack of enablement, it is unnecessary for us to address the Board's ruling regarding lack of adequate written description.

III

Rasmusson next argues that the pertinent claims of SmithKline's patents and reissue applications are invalid in light of the European application, EP '383.

In conjunction with filing his first application in the United States for finasteride, Rasmusson also filed EP '383. That application was published on October 5, 1988, between the filing dates of Rasmusson's second and third applications, and more than one year before the priority date assigned to SmithKline's patents and reissue patent applications. Before the Board, Rasmusson argued that EP '383 anticipated and rendered obvious all of SmithKline's claims at issue in this interference. The Board found, however, that EP '383 does not anticipate those claims because EP '383 lacks an enabling disclosure inasmuch as it fails to demonstrate that finasteride is effective in treating prostate cancer. The Board also found that EP '383 does not render the claims of the SmithKline patents and reissue applications invalid for obviousness, because it provides no reasonable expectation of success for treating prostate cancer with a 5 R inhibitor.

[6][7] A patent claim "cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." *Elan Pharm., Inc. v. Mayo Found. for Med. Educ. & Research*, 346 F.3d 1051, 1054 (Fed.Cir.2003). The standard for what constitutes proper enablement of a prior art reference for purposes of anticipation under section 102, however, differs from the enablement standard under section 112. In *In re Hafner*, 56 C.C.P.A. 1424, 410 F.2d 1403 (Cust. & Pat.App.1969), the court stated that "a disclosure lacking a teaching of how to use a fully disclosed compound for a specific, substantial utility or of how to use for such purpose a compound produced by a fully disclosed process is, under the present state of the law, entirely adequate to anticipate a claim to either the product or the process and, at the same time, entirely inadequate to support the allowance of such a claim." *Id.* at 1405; *see Schoenwald*, 964 F.2d at 1124; *In re Samour*, 571 F.2d 559, 563-64 (Cust. & Pat.App.1978). The reason is that section 112 "provides that the specification must enable one skilled in the art to 'use' the invention whereas [section] 102 makes no such requirement as to an anticipatory disclosure." *Hafner*, 410 F.2d at 1405; *see* 1 Donald S. Chisum, *Chisum on Patents* § 3.04[1][c] (2002); *see also In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349-52 (Fed.Cir.2002) (finding anticipation where applicant sought a patent based on a new use for a previously disclosed method).

***1326** [8] Since *Hafner,* this court has continued to recognize that a prior art reference need not demonstrate utility in order to serve as an anticipating reference under section 102. *See Schoenwald*, 964 F.2d at 1124 ("it is beyond argument that no utility need be disclosed for a reference to be anticipatory of a claim"); *In re Donohue*, 632 F.2d 123, 126 n. 6 (Cust. & Pat.App.1980) ("proof of utility is not a prerequisite to availability of a prior art reference under 35 U.S.C. § 102(b)"), *citing In re Samour*, 571 F.2d at 563-64; *see also Application of Lukach*, 58 C.C.P.A. 1233, 442 F.2d 967, 969 (Cust. & Pat.App.1971) (recognizing that there are "anomalies between the requirements for claim-anticipating disclosures and for claim-supporting disclosures" and citing *Hafner* as an example).

[9] The parties disagree about the significance of *Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368 (Fed.Cir.2001), in which this court held that a scientific article anticipated claims to a method for treating cancer by administering a particular drug. SmithKline argues that the case merely stands for the proposition that a reference must be enabling in order to anticipate under 35 U.S.C. § 102. Rasmusson, however, asserts that the case stands for the broader proposition that proof of efficacy is not required in order for a reference to be enabled for purposes of anticipation.

We agree with Rasmusson. In the *Bristol-Myers Squibb* case, the article and the patent disclosed the same method for administering the drug. The article, however, presented data purporting to show that the method was not effective in providing anti-tumor effects, while the patent contained data purporting to show the opposite. The court decided that the negative results reported in the article did not prevent the article from anticipating the patent given that "[n]ewly discovered results of known processes directed to the same purpose are not patentable because such results are inherent." 236 F.3d at 1376. The court explained that "a reference is no less anticipatory if, after disclosing the invention, the reference then disparages it. Thus, the question whether a reference 'teaches away' from the invention is inapplicable to an anticipation analysis." *Id.* at 1378, *quoting* *Celeritas Techs., Ltd. v. Rockwell Int'l Group*, 150 F.3d 1354, 1361 (Fed.Cir.1998). The court added that "anticipation does not require actual performance of suggestions in a disclosure." 246 F.3d at 1379.

[10] In this case, the Board found (1) that in light of the state of the art at the time of the publication of EP '383 in 1988, there was no reasonable scientific basis for a person of ordinary skill in the art to conclude that the claimed method would be effective in treating prostate cancer, and (2) that given the lack of proof provided in the publication itself, a person of ordinary skill in the art as of the publication date of EP '383 would not have believed that the method described in EP '383 would be effective. Under the legal standard set forth in *Hafner* and the cases that have followed it, those findings are insufficient to support the Board's conclusion that EP '383 is not an enabling reference for purposes of anticipation. Because the Board erred in ruling that EP '383 was not enabled for purposes of anticipation, we reverse the Board on that issue. Rasmusson argues that EP '383 discloses every limitation of SmithKline's claims at issue in the interference. SmithKline does not expressly challenge that contention, and Rasmusson accordingly urges us to rule that SmithKline's claims are anticipated. However, we consider that the preferable course is to allow the Board to resolve the anticipation question in the first instance. We therefore remand the case for the Board to rule on anticipation in light of our enablement decision. In light of our decision on anticipation, we do not address ***1327** Rasmusson's argument that the Board erred in finding that SmithKline's claims were not shown to have been obvious in light of EP '383.

IV

Our determination that EP '383 is an enabling reference has significant ramifications for Rasmusson's '296 patent application. Under section 102, an invention is not patentable if it was "described in a printed publication in this or a foreign country ... more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b). EP '383 was published on October 5, 1988, and we have determined that the '296 application is entitled to priority only as of June 2, 1995, the filing date of the ninth application. EP '383 was therefore published more than one year before that filing date. In view of the versions of the applications submitted to this court on appeal, EP '383 and the '296 application appear to share the same disclosure. We leave it to the Board, however, to make the factual determination of whether EP '383 and the '296 application disclose the same invention, and we therefore remand to the Board to determine whether EP '383 invalidates the '296 application under section 102(b). Finally, because we are upholding the Board's priority determination, we need not address SmithKline's conditional cross-appeal, in which SmithKline challenges the Board's denial of SmithKline's motion seeking to broaden the count in interference to include the use of selective 5 R inhibitors as a class.

Each party shall bear its own costs for this appeal.

AFFIRMED-IN-PART, REVERSED-IN-PART, and REMANDED.

C.A.Fed.,2005.
Rasmusson v. SmithKline Beecham Corp.

413 F.3d 1318, 75 U.S.P.Q.2d 1297
(Cite as: 413 F.3d 1318)

413 F.3d 1318, 75 U.S.P.Q.2d 1297

END OF DOCUMENT

583 F.3d 1317, 92 U.S.P.Q.2d 1385
(Cite as: 583 F.3d 1317)

United States Court of Appeals,
Federal Circuit.
In re '318 PATENT INFRINGEMENT LITIGATION.
Janssen Pharmaceutica N.V., Janssen L.P., and Synaptech, Inc., Plaintiffs-Appellants,
v.
Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries, Ltd., Defendants,
and
Mylan Pharmaceuticals, Inc. and Mylan Laboratories, Inc., Defendants-Appellees,
and
Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd., Defendants,
and
Barr Laboratories, Inc., Defendant-Appellee,
and
Purepac Pharmaceutical Co. and Actavis Group, Defendants,
and
Alphapharm Pty Ltd., Defendant-Appellee.
Janssen Pharmaceutica, N.V., Janssen, L.P., Ortho-Mcneil Neurologics, Inc., and Synaptech, Inc., Plaintiffs-Appellants,
v.
Barr Laboratories, Inc., and Barr Pharmaceuticals, Inc., Defendants-Appellees.

Nos. 2008-1594, 2009-1070, 2009-1088.
Sept. 25, 2009.

Background: Exclusive licensees of patent claiming a method for treating Alzheimer's disease with galanthamine brought infringement actions against several generic drug manufacturers. After the actions were consolidated and the drug manufacturers conceded infringement, the United States District Court for the District of Delaware, Sue L. Robinson, J., 578 F.Supp.2d 711, found the patent invalid for lack of enablement. Exclusive licensees appealed. Appeal was also taken from order of the United States District Court for the District of New Jersey, Joel A. Pisano, J., which entered judgment in related action.

Holding: The Court of Appeals, Dyk, Circuit Judge, held that patent was invalid for lack of enablement.

Affirmed.

Gajarsa, Circuit Judge, filed a dissenting opinion.

West Headnotes

[1] Patents 291 324.5

291 Patents
291XII Infringement
291XII(B) Actions
291k324 Appeal
291k324.5 k. Scope and extent of review in general. Most Cited Cases

Enablement of a patent is a question of law the Court of Appeals for the Federal Circuit reviews without deference. 35 U.S.C.A. § 112.

[2] Patents 291 324.55(2)

291 Patents
291XII Infringement
291XII(B) Actions
291k324 Appeal
291k324.55 Questions of Fact, Verdicts, and Findings
291k324.55(2) k. Clearly erroneous findings. Most Cited Cases

Court of Appeals for the Federal Circuit reviews the factual issues underlying enablement of a patent for clear error. 35 U.S.C.A. § 112.

[3] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Enablement is determined as of the effective filing date of the patent's application. 35 U.S.C.A. § 112.

[4] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Enablement is closely related to patent law's requirement for utility. 35 U.S.C.A. § 112.

[5] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Patent law's enablement requirement requires that the specification adequately disclose to one skilled in the relevant art how to make, or in the case of a process, how to carry out, the claimed invention without undue experimentation. 35 U.S.C.A. § 112.

[6] Patents 291 47

291 Patents
291II Patentability
291II(C) Utility
291k47 k. Capacity to produce result. Most Cited Cases

Patent law's utility requirement mandates that any patentable invention be useful and, accordingly, the subject matter of the claim must be operable. 35 U.S.C.A. § 101.

[7] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

If a patent claim fails to meet the utility requirement because it is not useful or operative, then it also fails to meet the how-to-use aspect of the enablement requirement. 35 U.S.C.A. §§ 101, 112.

[8] Patents 291 46

291 Patents
291II Patentability
291II(C) Utility
291k46 k. Nature and necessity of patentable utility. Most Cited Cases

Patent law's utility requirement prevents mere ideas from being patented. 35 U.S.C.A. § 101.

[9] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable; tossing out the mere germ of an idea does not constitute enabling disclosure. 35 U.S.C.A. § 112.

[10] Patents 291 46

291 Patents
291II Patentability
291II(C) Utility
291k46 k. Nature and necessity of patentable utility. Most Cited Cases

Patent law's utility requirement prevents the patenting of a mere research proposal or an invention that is simply an object of research. 35 U.S.C.A. § 112.

[11] Patents 291 1

291 Patents
291I Subjects of Patents
291k1 k. Nature of patent rights. Most Cited Cases

A patent is not a hunting license; it is not a reward for the search, but compensation for its successful conclusion.

[12] Patents 291 46

291 Patents

291II Patentability
291II(C) Utility
291k46 k. Nature and necessity of patentable utility. Most Cited Cases

A process or product which either has no known use or is useful only in the sense that it may be an object of scientific research is not patentable.

[13] Patents 291 46

291 Patents
291II Patentability
291II(C) Utility
291k46 k. Nature and necessity of patentable utility. Most Cited Cases

Inventions do not meet patent law's utility requirement if they are objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end; allowing ideas, research proposals, or objects only of research to be patented has the potential to give priority to the wrong party and to confer power to block off whole areas of scientific development, without compensating benefit to the public. 35 U.S.C.A. § 101.

[14] Patents 291 48

291 Patents
291II Patentability
291II(C) Utility
291k48 k. Nature of product or result. Most Cited Cases

Typically, patent applications claiming new methods of treatment are supported by test results; but testing need not be conducted by the inventor.

[15] Patents 291 49

291 Patents
291II Patentability
291II(C) Utility
291k49 k. Evidence of utility. Most Cited Cases

Human trials are not required for a therapeutic invention to be patentable.

[16] Patents 291 46

291 Patents
291II Patentability
291II(C) Utility
291k46 k. Nature and necessity of patentable utility. Most Cited Cases

Were human trials required in order to prove utility of a patent, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue potential cures. 35 U.S.C.A. § 101.

[17] Patents 291 99

291 Patents
291IV Applications and Proceedings Thereon
291k99 k. Description of invention in specification. Most Cited Cases

Specification of patent claiming a method for treating Alzheimer's disease with galanthamine failed to convey required assertion of a credible utility, and thus patent was invalid for lack of enablement. 35 U.S.C.A. §§ 101, 112.

[18] Federal Courts 170B 848

170B Federal Courts
170BVIII Courts of Appeals
170BVIII(K) Scope, Standards, and Extent
170BVIII(K)5 Questions of Fact, Verdicts and Findings
170Bk848 k. Findings of court in general. Most Cited Cases

Where disputed factual findings are irrelevant, it is not error not to make them. 28 U.S.C.A. § 2111.

Patents 291 328(2)

291 Patents
291XIII Decisions on the Validity, Construction, and Infringement of Particular Patents
291k328 Patents Enumerated
291k328(2) k. Original utility. Most Cited Cases

4,663,318. Invalid.

***1319** George F. Pappas, Covington & Burling LLP, of Washington, DC, argued for all plaintiffs-appellants. With him on the ***1320** brief for Janssen Pharmaceutica, N.V., et al. were Christopher N. Sipes and Kurt G. Calia. Of counsel on the brief for plaintiff-appellant Synaptech, Inc. were Edward V. Filardi and Rachel Blitzer, Skadden, Arps, Slate, Meagher & Flom LLP, of New York, NY.

William A. Rakoczy, Rakoczy Molino Mazzochi Siwik LLP, of Chicago, IL, argued for defendants-appellees Mylan Pharmaceuticals, Inc., Mylan Laboratories, Inc., and Alphapharm Pty Ltd. With him on the brief for defendants-appellees Mylan Pharmaceuticals, Inc., et al. were Christine J. Siwik and Amy D. Brody; Mona Gupta, Alan H. Bernstein, James J. Kozuch, and William C. Youngblood, Caesar Rivise Bernstein Cohen & Pokotilow, Ltd., of Philadelphia, Pennsylvania, for defendant-appellee Alphapharm Pty Ltd.

George C. Lombardi, Winston & Strawn LLP, of Chicago, IL, argued for defendant-appellee Barr Laboratories, et al. With him on the brief were Taras A. Gracey, Lynn M. Ulrich, Ryanne L. Easley and William P. Ferranti. Of counsel was Steven J. Winger.

Before MAYER, GAJARSA, and DYK, Circuit Judges.

DYK, Circuit Judge.

Janssen Pharmaceutica N.V., Janssen L.P., and Synaptech, Inc. ("Janssen"), appeal from a final judgment of the United States District Court for the District of Delaware. After a bench trial, the district court determined that the claims of U.S. Patent No. 4,663,318 ("the '318 patent") were invalid for lack of enablement. *In re '318 Patent Infringement Litig.*, 578 F.Supp.2d 711, 737 (D.Del.2008). We affirm.

BACKGROUND

Janssen's '318 patent claims a method for treating Alzheimer's disease with galanthamine. Claim 1 is representative. It claims "[a] method of treating Alzheimer's disease and related dementias which comprises administering to a patient suffering from such a disease a therapeutically effective amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof." '318 patent col.3 ll.6-10.[FN1] The application for the '318 patent was filed on January 15, 1986, by Dr. Bonnie Davis, the claimed inventor.

FN1. The six additional claims in the '318 patent claim the administration of galantamine orally, parenterally, or intracerebroventricularly in various dosage ranges.

Alzheimer's disease is a form of progressive dementia in which memory and mental abilities steadily decline. At the time of the '318 patent's application in early 1986, researchers had observed a correlation between Alzheimer's disease symptoms and a reduced level of the neurotransmitter acetylcholine in the brain. During neurotransmission, acetylcholine is released by a transmitting neuron and binds to receptors on a receiving neuron. The two main types of acetylcholine receptors are nicotinic receptors and muscarinic receptors. Nicotinic and muscarinic receptors are present in neurons in both the central nervous system (which includes the brain and spinal cord) and the peripheral nervous system (which connects the central nervous system to muscles and organs).

In early 1986, many researchers focused primarily on the importance of central nervous system muscarinic receptors in developing treatments for Alzheimer's disease. At that time, galanthamine (also spelled "galantamine"), a small molecule compound, was known to inhibit acetylcholinesterase, an enzyme that breaks down acetylcholine. Acetylcholinesterase inhibitors like galantamine increase the amount ***1321** of acetylcholine available for binding to muscarinic or nicotinic receptors.

The specification for the '318 patent was only just over one page in length, and it provided almost no basis for its stated conclusion that it was possible to administer "an effective Alzheimer's disease cognitively-enhancing amount of galanthamine." *Id.* col.1 ll.47-48. The specification provided short summaries of six scientific papers in which galantamine had been administered to humans or animals.[FN2] The specification summarized the first paper as showing that administering galantamine with the drug atropine to humans under anesthesia raised blood levels of the hormone cortisol, and the second paper as showing that administering galantamine and atropine together

during anesthesia also raised levels of adrenocorticotropic hormone ("ACTH") in humans. *See id.* col.1 ll.13-21. There was no explanation of the significance of increasing cortisol or ACTH levels, but it was known to those skilled in the art in early 1986 that the production of cortisol and ACTH was controlled by the central nervous system rather than the peripheral nervous system, and that the studies thus suggested that galantamine was able to cross the blood-brain barrier and have effects within the brain.

FN2. The specification stated:

> Galanthamine and acid addition salts thereof have, for many years, been known to have anticholinesterase properties. Cozanitis in Anaesthesia 29 163-8 (1974) describes the effect of galanthamine hydrobromide on plasma cortisol of patients receiving relaxant anaesthesia and Cozanitis et al in Acta Anesth. Scand. 24:166-168 (1980) describe the effect of galanthamine on plasma ACTH values during anaethesia. These studies showed an increase in both plasma cortisol and plasma ACTH when galanthamine was administered to patients together with atropine.
>
> Il'yuchenok et al (Chemical Abstracts 70 36296K) describe the appearance of *è*-rhythm on an electroencephalogram when galanthamine is administered intravenously to rabbits.
>
> Increase in short-term memory in dogs by use of galanthamine is described by Krauz in Chemical Abstracts 81 72615Z.
>
> The antagonistic effect of galanthamine to scopolamine-induced amnesia in rats is described by Chaplygina et al in Chemical Abstracts 86 115157Z, and in Zhurnal Vysshei Nervnoi Deiatelnosti imeni P. Pavlova (MOSKVA) 26:1091-1093, 1976.
>
> '318 patent col.1 ll.11-33.

The specification then provided brief summaries of four scientific papers reporting brain effects and positive effects on memory from administering galantamine to animals. *See id.* col.1 ll.22-33. The first paper concluded that galantamine intravenously administered to rabbits affected brain wave activity. The second paper concluded that galantamine increased short-term memory in dogs. The third and fourth papers concluded that galantamine reversed amnesia in rats that had been induced by administering the drug scopolamine. The specification did not suggest that such scopolamine-induced amnesia was similar to Alzheimer's disease. The specification did not provide analysis or insight connecting the results of any of these six studies to galantamine's potential to treat Alzheimer's disease in humans.

The specification noted that another prior art scientific paper described an animal testing model for replicating in animals the acetylcholine deficit and other effects of Alzheimer's disease.[FN3] The specification ***1322** agreed that acetylcholine deficiency in animals is a "good animal model for Alzheimer's disease in humans" because the deficiency produces "[n]umerous behavioral deficits, including the inability to learn and retain new information." *Id.* col.2 ll.50-52. The specification cited the prior art for the conclusion that "[d]rugs that can normalize these abnormalities would have a reasonable expectation of efficacy in Alzheimer's disease." *Id.* col.2 ll.52-54. However, the specification did not refer to any then-existing animal test results involving the administration of galantamine in connection with this animal model of Alzheimer's disease.

FN3. The specification of the '318 patent stated:

> The following test provides a good animal model for Alzheimer's disease in humans: A selective lesion is placed in a subcortical nucleus (nucleus basalis of Meynert) with a resultant cortical cholinergic [i.e., acetylcholine] deficiency, similar in magnitude to that seen in early to moderate stage Alzheimer's disease. Numerous behavioral deficits, including the inability to learn and retain new information, characterizes this lesion. Drugs that can normalize these abnormalities would have a reasonable expectation of efficacy in Alzheimer's disease. Haroutunian, V, Kanof P, Davis, KL: Pharmacological alleviations of cho-

> linergic-lesion-induced memory defects in rats. Life Sciences 37:945-952, 1985.
>
> '318 patent col.2 ll.45-57.

In April 1986 an examiner at the United States Patent and Trademark Office ("PTO") rejected the claims in the '318 patent's application for indefiniteness and obviousness. The examiner found the patent application's claim of a method of "diagnosing" Alzheimer's disease to be indefinite, because diagnosing "has nothing to do with treating" and because the claims thus "fail[ed] to particularly point out and distinctly claim the subject matter which applicant regards as the invention." J.A. 4108. The examiner also found the patent application's claim of a method of treating Alzheimer's disease obvious-in light of the animal studies cited in the specification describing the use of galantamine to treat scopolamine-induced amnesia and in improving short-term memory. The examiner did not reject the application for lack of enablement.

In September 1986 the applicant, Dr. Davis, responded to the examiner's indefiniteness rejection by narrowing the claim language, deleting the words "and diagnosing" from the original application's claim of "[a] method of treating and diagnosing Alzheimer's disease." Dr. Davis responded to the obviousness rejection by explaining that, because the brains of the animals in the studies cited in the specification were "normal" (rather than having "physiological changes" similar to Alzheimer's disease), the studies were conducted under "circumstances having no relevance to Alzheimer's disease," and that it thus would be "baseless" to predict from such studies that galantamine would be useful to treat Alzheimer's disease. J.A. 4407.

In addition, Dr. Davis responded by stating that "experiments [are] underway using animal models which are expected to show that treatment with galanthamine does result in an improvement in the condition of those suffering from Alzheimer's disease," and that it was "expected that data from this experimental work will be available in two to three months and will be submitted to the Examiner promptly thereafter." J.A. 4405. The '318 patent issued on May 5, 1987. Dr. Davis did not learn the results of the animal testing experiments-which suggested that galantamine could be a promising Alzheimer's disease treatment-until July 1987, after the '318 patent had issued. These studies required several months and considerable effort by researchers at the Johns Hopkins University under the supervision of Dr. Joseph T. Coyle. No such testing results were ever submitted to the PTO.

After the '318 patent issued in May 1987, Dr. Davis licensed the patent in November 1995 to Janssen. In February 2001 Janssen received approval from the Food and Drug Administration ("FDA") for using galantamine to treat mild to moderate Alzheimer's disease.

***1323** In February 2005 several generic drug manufacturers filed abbreviated new drug applications ("ANDAs") and so-called "Paragraph IV" certifications with the FDA, and Janssen sued each manufacturer for infringing the '318 patent.[FN4] The actions were consolidated, the defendants conceded infringement of claims 1 and 4 of the '318 patent, and a bench trial was held in May 2007 on the invalidity issues of anticipation, obviousness, and enablement.

> FN4. A Paragraph IV certification "is defined as an act of infringement for litigation purposes." *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1078 (Fed.Cir.2008); *see* 21 U.S.C. § 355(j)(2)(A)(vii)(IV); 35 U.S.C. § 271(e).

The district court found that the '318 patent was neither anticipated nor obvious. However, the district court concluded that the '318 patent was invalid for lack of enablement on two distinct grounds. The district court found that the specification did not demonstrate utility because relevant animal testing experiments were "not finished ... by the time the '318 patent was allowed" and the specification provided only "minimal disclosure" of utility. *'318 Patent Infringement Litig.*, 578 F.Supp.2d at 723, 735; *see also id.* at 736-37 & n. 39. The district court alternatively found that the specification and claims did not "teach one of skill in the art how to use the claimed method" because the application "only surmise[d] how the claimed method could be used" without providing sufficient galantamine dosage information. *Id.* at 736. The district court entered judgment in favor of the defendants that the '318 patent was invalid for lack of enablement.

Janssen timely appealed. We have jurisdiction under 28 U.S.C. §§ 1291 and 1295(a)(1).

DISCUSSION

[1][2] Enablement is a question of law we review without deference. *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052, 1070 (Fed.Cir.2005). We review the factual issues underlying enablement for clear error. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1369 (Fed.Cir.1999).

[3] The enablement requirement is stated in 35 U.S.C. § 112. [FN5] Enablement is determined as of the effective filing date of the patent's application. *Plant Genetic Sys., N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1339 (Fed.Cir.2003).

FN5. The statute states:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms *as to enable any person skilled in the art* to which it pertains, or with which it is most nearly connected, *to make and use the same*, and shall set forth the best mode contemplated by the inventor of carrying out his invention.
>
> 35 U.S.C. § 112, ¶ 1 (emphases added).

[4][5][6][7] Enablement is closely related to the requirement for utility. [FN6] As we noted in *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1358 (Fed.Cir.1999),

FN6. The utility requirement is stated in 35 U.S.C. § 101:

> Whoever invents or discovers any new and *useful* process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
>
> (emphases added).

> The enablement requirement of 35 U.S.C. § 112, ¶ 1 requires that the specification adequately discloses to one skilled in the relevant art how to make, or in the case of a process, how to carry out, the claimed invention without undue experimentation. The utility requirement of 35 U.S.C. § 101 mandates that ***1324** any patentable invention be useful and, accordingly, the subject matter of the claim must be operable. *If a patent claim fails to meet the utility requirement because it is not useful or operative, then it also fails to meet the how-to-use aspect of the enablement requirement.*
> (emphasis added, citations and footnote omitted). *See also* 3 Donald A. Chisum, *Chisum on Patents* § 7.03(6) (2007). The Supreme Court in *Brenner v. Manson*, 383 U.S. 519, 86 S.Ct. 1033, 16 L.Ed.2d 69 (1966), discussing the utility requirement, stated that inventions must have "substantial utility" and "specific benefit exist[ing] in currently available form." *Id.* at 534-35, 86 S.Ct. 1033.

[8][9] The utility requirement prevents mere ideas from being patented. As we noted in *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed.Cir.1997), "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.... Tossing out the mere germ of an idea does not constitute enabling disclosure." *See also In re Fisher*, 421 F.3d 1365, 1373 (Fed.Cir.2005) (inventions fail to meet the utility requirement if their "asserted uses represent merely hypothetical possibilities, objectives which the claimed [inventions] ... *could* possibly achieve, but none for which they have been used in the real world").

[10][11][12][13] The utility requirement also prevents the patenting of a mere research proposal or an invention that is simply an object of research. Again as the Supreme Court stated in *Brenner*, "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." 383 U.S. at 536, 86 S.Ct. 1033. A process or product "which either has no known use or is useful only in the sense that it may be an object of scientific research" is not patentable. *Id.* at 535, 86 S.Ct. 1033. As we observed in Fisher, inventions do not meet the utility requirement if they are "objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end." 421 F.3d at 1373. Allowing ideas, research proposals, or objects only of research to be patented

has the potential to give priority to the wrong party and to "confer power to block off whole areas of scientific development, without compensating benefit to the public." *Brenner*, 383 U.S. at 534, 86 S.Ct. 1033 (footnote omitted).

[14][15][16] Typically, patent applications claiming new methods of treatment are supported by test results. But it is clear that testing need not be conducted by the inventor. In addition, human trials are not required for a therapeutic invention to be patentable. Our predecessor court, the United States Court of Customs and Patent Appeals, held in *In re Krimmel* that patent applications need not "prove that compounds or other materials which [the applicant] is claiming, and which [the applicant] has stated are useful for 'pharmaceutical applications' are safe, effective, and reliable for use with humans." 48 C.C.P.A. 1116, 292 F.2d 948, 954 (Cust. & Pat.App.1961). As we observed in *In re Brana*, "[w]ere we to require Phase II testing [human trials] in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue ... potential cures." 51 F.3d 1560, 1568 (Fed.Cir.1995); *see also Scott v. Finney*, 34 F.3d 1058, 1063-64 (Fed.Cir.1994).

We have held that results from animal tests or in vitro experiments [FN7] may be sufficient***1325** to satisfy the utility requirement. Our predecessor court held in *Krimmel* that animal tests showing that a new nonobvious compound "exhibits some useful pharmaceutical property" are sufficient to demonstrate utility. 292 F.2d at 953. We noted in *Cross v. Iizuka* that "[w]e perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the [pharmaceutical] compound in question" in order for a patent to issue. 753 F.2d 1040, 1051 (Fed.Cir.1985). We concluded that in vitro test results for a claimed pharmaceutical compound, combined with animal test results for a structurally similar compound, showed "a reasonable correlation between the disclosed *in vitro* utility and an in vivo activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence." *Id.* at 1050.

FN7. "In vitro" experiments are performed in artificial environments outside living organisms (such as in a test tube or culture media), while "in vivo" experiments are performed within living organisms. *Brana*, 51 F.3d at 1562 n. 3; *Cross v. Iizuka*, 753 F.2d 1040, 1043 n. 6 (Fed.Cir.1985).

[17] In this case, however, neither in vitro test results nor animal test results involving the use of galantamine to treat Alzheimer's-like conditions were provided. The results from the '318 patent's proposed animal tests of galantamine for treating symptoms of Alzheimer's disease were not available at the time of the application, and the district court properly held that they could not be used to establish enablement.[FN8]

FN8. In *Brana* we held that the patent applicants had established the utility of claimed therapeutic compounds by presenting in vitro test results and evidence of structural similarity between the claimed and prior art compounds when filing the application. 51 F.3d at 1566. The applicants also submitted animal testing results for the claimed compounds to the PTO after the filing date, but our finding of enablement did not depend on these post-application test results. In *Brana*, moreover, unlike the present case, the testing was submitted to the PTO during prosecution. *Id.* at 1567.

Nor does Janssen contend that the prior art animal testing summarized in the ' 318 patent application's specification established utility. Indeed, both in responding to the examiner's obviousness rejection and in responding to the obviousness defense at trial, the inventor (Dr. Davis) and Janssen's witnesses explicitly stated that the utility of the invention could not be inferred from the prior art testing described in the application. The response of the inventor, Dr. Davis, to the examiner's obviousness rejection stated, with regard to studies cited in the specification showing galantamine's ability to reverse scopolamine-induced amnesia in normal rats, that "[n]othing in this teaching leads to an expectation of utility against Alzheimer's disease." J.A. 4409. The response of Dr. Davis also stated that "predict[ing] that galanthamine would be useful in treating Alzheimer's disease just because it has been reported [in the prior art studies cited in the specification] to have an effect on memory in circumstances having no relevance to Alzheimer's dis-

ease" would be "as baseless as a prediction that impaired eyesight due to diabetes would respond to devices (eyeglasses) or treatments (eye exercises) known to improve the vision of normal persons." J.A. 4407. Janssen's other expert Dr. Raskind testified that studying a compound's effects on scopolamine-induced amnesia "ignores the whole other [nicotinic] part that's damaged in Alzheimer's disease" and thus "doesn't mimic Alzheimer's disease." J.A. 9301-02. The district court agreed, finding, for example, that the utility of galantamine in treating scopolamine-induced amnesia did ***1326** not establish galantamine's utility in treating Alzheimer's disease. *See '318 Patent Infringement Litig.*, 578 F.Supp.2d at 731 ("[S]copolamine ['s] ... usefulness as a model for [Alzheimer's disease] research has limitations.... [A] person of skill in the art would not have a reasonable expectation of success for using a drug that worked for scopolamine-induced delirium to treat [Alzheimer's disease].").

However, Janssen argues that in some circumstances utility may be established without testing the proposed treatment in the claimed environment or a sufficiently similar or predictive environment; that is, Janssen argues that utility may be established by analytic reasoning. Although no case has been called to our attention where utility was established simply by analytic reasoning,[FN9] the PTO's Manual of Patent Examining Procedure ("MPEP") has recognized that "arguments or reasoning" may be used to establish an invention's therapeutic utility.[FN10]

> FN9. Cases cited by Janssen did not involve patents that relied solely on analysis to establish utility. *See, e.g.*, *Brana*, 51 F.3d at 1565-66 (holding that patent applicants had established the utility of claimed therapeutic compounds by presenting in vitro test results and evidence of structural similarity to therapeutically useful compounds); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576-77 (Fed.Cir.1984) (upholding a district court's judgment of enablement because the examples in the specification "were based on actual experiments").

> FN10. As stated in the MPEP, establishing "a reasonable correlation between" a compound's activity and its asserted therapeutic use may involve "statistically relevant data documenting the activity of a compound or composition, arguments or reasoning, documentary evidence (e.g., articles in scientific journals), or any combination thereof." MPEP § 2107.03 (8th ed., Rev.7, July 2008). *See also Fisher*, 421 F.3d at 1372 ("The MPEP and [PTO Utility] Guidelines are not binding on this court, but may be given judicial notice to the extent they do not conflict with the statute." (quotation marks omitted)).

Janssen goes on to argue that the specification here establishes utility by analytic reasoning. Relying on trial testimony, Janssen reasons that the selection and description of the prior art tests, while not directly pertinent, "set[ ] forth the evidence from existing studies demonstrating galantamine's effects on central nicotinic as well as muscarinic receptors and connect[ed] it to a model for Alzheimer's therapy rendering those effects therapeutically relevant." Janssen Reply Br. 17 n. 2. Janssen asserts that the prior art tests summarized in the specification would lead one skilled in the art to infer that galantamine affected the ability of acetylcholine to bind to both nicotinic and muscarinic receptors in the brain. Janssen also asserts that the animal tests proposed in the specification as a model for Alzheimer's disease would further lead one skilled in the art to infer that the model's method of impairing brain acetylcholine availability would allow both muscarinic and nicotinic effects to be observed. Janssen thus argues that because nicotinic receptors in the brain are involved with the ability to learn, the specification suggested that galantamine could have beneficial effects on learning (unlike prior art treatments, which had primarily affected muscarinic receptors). These insights, however, are nowhere described in the specification. Nor was there evidence that someone skilled in the art would infer galantamine's utility from the specification, even if such inferences could substitute for an explicit description of utility.

Janssen relies on the testimony of its expert Dr. Coyle, the scientist who later supervised the performance of the animal studies suggested in the specification. He testified that the specification "connected the dots" for galantamine as a potential Alzheimer's disease treatment, listing the "dots" as "[g]alanthamine in humans safe ***1327** and well tol-

erated [,][c]holinesterase inhibitor, selective nicotinic effects, and very modest muscarinic receptor side effects." J.A. 9057-58. This testimony of Dr. Coyle on which Janssen relies, however, characterized the use of galantamine to treat Alzheimer's disease as "a *proposal* that connected the dots that raised very interesting questions and *worth the effort to check it out* in a model in which ... both nicotinic and muscarinic receptors would come into play." *Id.* (emphases added).[FN11] Similarly, agreement by another of Janssen's expert witnesses, Dr. Raskind, that a person of ordinary skill in the art in early 1986 would have viewed the "invention as set forth in the patent as scientifically grounded" falls far short of demonstrating that a person of ordinary skill in the art would have recognized that the specification conveyed the required assertion of a credible utility. J.A. 9305. In fact, the inventor's own testimony reveals that an ordinarily skilled artisan would not have viewed the patent's disclosure as describing the utility of galantamine as a treatment for Alzheimer's disease: "[W]hen I submitted this patent, I certainly wasn't sure, and a lot of other people weren't sure that cholinesterase inhibitors[, a category of agents that includes galantamine,] would ever work." J.A. 8747; *see In re '318 Patent Infringement Litig.*, 578 F.Supp.2d at 736.

> FN11. Janssen also relies on conclusory testimony by defendants' witness Dr. Levey to establish that the specification demonstrated utility. *See* J.A. 8329-30 (Dr. Levey agreeing that "the idea of using galanthamine as a treatment[ ] for Alzheimer's disease in 1986 [was a] scientifically reasonable judgment"). The testimony by defendants' witness Dr. Levey was in support of an obviousness defense and was not credited by the district court, and Dr. Levey testified that if the district court rejected his opinion that the '318 patent was obvious, then it was his opinion that the patent was not enabled. *See* J.A. 8248, 8253.

Thus, at the end of the day, the specification, even read in the light of the knowledge of those skilled in the art, does no more than state a hypothesis and propose testing to determine the accuracy of that hypothesis. That is not sufficient. *See Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1325 (Fed.Cir.2005) ("If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis.").

[18] The '318 patent's description of using galantamine to treat Alzheimer's disease thus does not satisfy the enablement requirement because the '318 patent's application did not establish utility.[FN12]

> FN12. Under circumstances where the record would not support a finding of utility, the absence of findings by the district court on the issue of whether a person skilled in the art could infer galantamine's utility from the selected prior art described in the '318 patent's specification is not error. Where disputed factual findings are irrelevant, it is not error not to make them. *See* 28 U.S.C. § 2111 ("On the hearing of any appeal ... the court shall give judgment after an examination of the record without regard to errors or defects which do not affect the substantial rights of the parties."); *Sampson v. Murray*, 415 U.S. 61, 87 n. 58, 94 S.Ct. 937, 39 L.Ed.2d 166 (1974) ("Admittedly, the District Court did not comply with Fed. Rule Civ. Proc. 52(a), but we do not think that we are thereby foreclosed from examining the record to determine if sufficient allegations or sufficient evidence supports the issuance of injunctive relief."); *Baxter Healthcare Corp. v. Spectramed, Inc.*, 49 F.3d 1575, 1582 (Fed.Cir.1995) (declining to remand because "[o]n appeal we are free to examine the record to determine whether the facts support the judgment"); *Consol. Aluminum Corp. v. Foseco Int'l Ltd.*, 910 F.2d 804, 814 (Fed.Cir.1990) ("[R]emand should not be a matter of rote in every case in which findings and reason are not expressly set forth. An appellate court need not close its eyes to the record where, as in this case, there is a way clearly open to affirm the district court's action."); *see also Jenkens & Gilchrist v. Groia & Co.*, 542 F.3d 114, 119 (5th Cir.2008)

("[A] remand is not necessary if the record would not support a finding ... and if such a finding would be deemed clearly erroneous had it been made." (quotation marks omitted)); *United States v. $242,484.00*, 389 F.3d 1149, 1154 (11th Cir.2004) ("We can and have decided appeals on the merits where the district court has not even entered any findings on each separate factual issue so long as a complete understanding of the issues is possible." (quotation marks omitted)).

***1328** CONCLUSION

For the foregoing reasons, the decision of the district court is affirmed.

AFFIRMED

COSTS

No costs.

GAJARSA, Circuit Judge, dissenting.

I respectfully dissent from the majority's affirmance because the district court did not undertake the required legal analysis to determine whether an ordinarily skilled artisan reading the patent would understand it to reveal a credible utility for the invention. In addition, the district court failed to make the factual findings necessary to support the ultimate legal conclusion regarding enablement. *See Koito Mfg. Co. v. Turn-Key-Tech, LLC*, 381 F.3d 1142, 1149 (Fed.Cir.2004) ("Enablement is a matter of law that we review without deference; however, this Court reviews the factual underpinnings of enablement for substantial evidence."). Thus, I would vacate the judgment of non-enablement and remand for the district court to make the required factual findings and to perform the necessary legal analysis in the first instance.

The parties do not dispute that Dr. Davis's insight regarding galantamine's utility for treating Alzheimer's Disease (AD) was correct; later animal studies and human clinical trials proved and confirmed galantamine's effectiveness. The relevant question here is whether, at the time Dr. Davis filed her application, the patent's written description would have credibly revealed to an ordinarily skilled artisan galantamine's utility for AD treatment. *See In re Cortright*, 165 F.3d 1353, 1356 (Fed.Cir.1999) (noting that the patent's written description must "illuminate a credible utility" to meet the enablement requirement). The district court failed to answer that question. Instead, the district court reasoned:

> Dr. Davis did not receive any confirming data until after the '318 patent was allowed. In view of the prior art disclosures regarding the flaws of physostigmine [a compound chemically similar to galantamine] in AD treatment, discussed previously in the context of obviousness, it does not follow that a person of ordinary skill in the art, reading the '318 patent, would have recognized that galanthamine would be effective in treating AD in the absence of any experimental proof. Put another way, since plaintiffs rely exclusively on the prior art to establish enablement, the court agrees with defendants that the '318 patent cannot both be non-obvious and enabled.

In re '318 Patent Infringement Litig., 578 F.Supp.2d 711, 736 (D.Del.2008) (citation and footnote omitted) (" *District Court Decision*").

The district court's reasoning is flawed. In general terms, an inventor may look at the prior art differently than those before her, arrive at a novel and nonobvious insight,***1329** and submit a patent application that compiles the prior art findings that led her to the insight in such a way as to render obvious in hindsight what was wholly nonobvious at the time she filed her application. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 420, 127 S.Ct. 1727, 167 L.Ed.2d 705 (2007) ("The question is not whether the combination was obvious to the patentee but whether the combination was obvious to a person with ordinary skill in the art."); *Grain Processing Corp. v. Am. Maize-Products Co.*, 840 F.2d 902, 907 (Fed.Cir.1988) (In considering obviousness, "[c]are must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.' " (quoting *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1012 (Fed.Cir.1983))). As a result, the proper focus when assessing enablement is on what is disclosed in the patent, not what is taught in the prior art. *See In re Ziegler*, 992 F.2d 1197, 1201 (Fed.Cir.1993) ("The how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 *that the specification disclose* as a matter of fact *a practical utility* for the invention." (emphases added)). In terms of the present case, if Dr. Davis used her unique

neuroendocrine perspective to examine the prior art and arrive at a novel insight about galantamine based on selected prior art findings, then the invention may be nonobvious; and if her patent disclosed those selected findings in such a manner that a person of ordinary skill would credit her insight regarding galantamine's utility, then the invention is enabled.

Unfortunately, the district court committed error here by focusing generally on what the prior art does or does not teach-the primary factual consideration underlying obviousness-while neglecting to consider what the patent text discloses to an ordinarily skilled artisan-the primary factual consideration underlying enablement. Specifically, although the '381 patent describes particular findings from six prior art publications, the district court noted only one such publication, *see District Court Decision*, 578 F.Supp.2d at 722, and did not determine how one of ordinary skill would understand those cited findings, either independently or in combination with one another. Thus, it is clear that the district court failed to focus on the necessary underlying factual findings required to ascertain how an ordinarily skilled artisan would understand the text of the patent for the purpose of establishing utility and thus enablement. Under the district court's erroneous approach, a court can invalidate for lack of enablement a patent claim to a nonobvious combination of prior art elements without ever considering what the patent actually discloses to one of ordinary skill in the art. That is contrary to law.

Nor was the district court's error harmless. *See* Majority Op. at at 1327-28 n. 12. Because the district court failed to make the required fact-findings, which stemmed from its erroneous legal analysis, the majority must engage in extensive appellate fact-finding in order to affirm the district court's judgment. It is improper for an appellate court to become the fact-finder. This court cannot presume to have the skills of the ordinary artisan and cannot substitute its weighing of the evidence and factual conclusions for those of the fact-finder. According to the majority, even though the district court failed to make the appropriate findings or conduct the proper legal analysis, we need not vacate here because "the record would not support a finding of utility." *Id.* I respectfully disagree. The record clearly includes evidence that may support a finding of utility, which the majority discounts in order to reach its ***1330** erroneous conclusion.[FN1] For example, Janssen provided evidence indicating that the specific findings recited in the patent, as understood by one of ordinary skill in the art, disclose the following: (1) galantamine administration increases blood cortisol levels and plasma acetylcholine when muscarinic function is blocked, an indication that galantamine increases the function of central nicotinic receptors, J.A. 8906-07; J.A. 9296-97; J.A. 9302-03; (2) galantamine can cross into the brain and affect brain function, J.A. 9298; J.A. 9303; (3) galantamine also has muscarinic effects in the brain, as indicated by its ability to improve memory in animals that have been administered scopolamine (a muscarinic receptor blocker) to induce amnesia, J.A. 8250; J.A. 8963; J.A. 9298-99; and (4) the patent discloses the importance of nicotinic receptors in AD by describing an animal model for AD that includes muscarinic *and* nicotinic receptors, J.A. 9302. Thus, one of ordinary skill-having the relevant background knowledge and reading the patent text at the time the application was filed-may have understood the patent to disclose the importance of nicotinic receptors in AD intervention and galantamine's promising effects on nicotinic function and memory, such that she would recognize in the patent text galantamine's credible utility as an AD treatment. Moreover, the defendants' expert agreed that "[a] person in 1986 reading the patent would believe that galanthamine would be a treatment for Alzheimer's Disease." J.A. 8327. Although the defendants' expert gave that testimony in support of his assertion that the claims are obvious, *see* Majority Op. at 1327 n. 11, the testimony is nonetheless evidence that may support a finding for the patentee on enablement. Because there is evidence of record that supports a conclusion that the '318 patent claims are not invalid, it is inappropriate for this ***1331** court to weigh the evidence and make contrary factual findings, especially in the absence of any consideration by the district court of numerous prior art references that were specifically discussed in the patent. Thus, in my judgment the district court's failure to make the necessary findings and conduct the proper legal analysis is reversible error. We should remand to the district court for it to make the appropriate factual findings instead of weighing the evidence ourselves.

> FN1. In particular, the majority discounts both the disclosures made in the '318 patent specification and the value of the post-filing test results offered to support a finding of credible utility. In so doing, the majority attempts to distinguish this court's decision in *In re Brana*, 51 F.3d 1560 (Fed.Cir.1995).

See Majority Op. at 1325 n. 8. I do not believe a distinction may so readily be made. Rather, as here, evidence of post-filing test results was presented to support a finding of utility. That evidence, the court found, "alone should have been sufficient to satisfy applicants' burden [even assuming the PTO had met its initial burden, thereby shifting the burden to applicants]." *Brana*, 51 F.3d at 1567. The majority's claim that "unlike the present case, the testing [in *Brana]* was submitted to the PTO during prosecution" is misleading. The appeal in Brana was taken from the Board of Patent Appeals to this court during prosecution of a patent application. And thus the *Brana* panel could not possibly have intended to provide for a distinction between test results offered to support the credible utility of an otherwise enabling disclosure pre- and post-patent issuance.

Moreover, the majority's relentless focus on the need for timely test results as evidence of utility appears to conflate credible utility in the context of enablement, at issue here, with the notion of reduction to practice, which is not at issue. *See, e.g.*, Majority Op. at 1326 ("[N]o case has been called to our attention where utility was established simply by analytic reasoning [without testing]."). Such a conflation risks the introduction of an actual reduction-to-practice requirement into patent law, contrary to more than a century of settled precedent. *See The Telephone Cases*, 126 U.S. 1, 536, 8 S.Ct. 778, 31 L.Ed. 863 (1888) ("The law does not require that a discoverer or inventor, in order to get a patent for a process, must have succeeded in bringing his art to the highest degree of perfection; it is enough if he describes his method with sufficient clearness and precision to enable those skilled in the matter to understand what the process is, and if he points out some practicable way of putting it into operation."). To reiterate: the question here is whether the written description of the '318 patent would have illuminated to a person of ordinary skill in the art a credible utility, not whether actual utility was in fact demonstrated.

Finally, I disagree with the majority opinion's emphasis on the sufficiency of the evidence presented by Janssen. As both parties correctly note, the question before us is "whether the defendants have shown, by clear and convincing evidence, that the patent's marshalling of evidence from the technical literature of galantamine's effects, combined with its model for Alzheimer's therapy, is not sufficient for a skilled artisan to believe the invention's utility." Appellant's Br. at 27; Appellee's Br. at 29. That is a correct articulation of the question presented on appeal because, unlike many of the cases upon which the majority and district court rely, the claims in dispute here are issued patent claims, and are thus presumed valid. Yet, the majority fails to establish the defendants' burden and instead focuses almost exclusively on the sufficiency of Janssen's showing and the merit of Janssen's arguments. *See, e.g.*, Majority Op. at 1327 ("Similarly, [the testimony of Janssen's expert witness, Dr. Raskind] falls far short of demonstrating that a person of ordinary skill in the art would have recognized that the specification conveyed the required showing of utility."). That focus is improper. Because the district court erred as a matter of law *and* failed to make certain required factual findings, we cannot defer to the district court's legal conclusion or fact-findings, and thus, it is particularly problematic for the majority to require Janssen to demonstrate on appeal that its patent is valid.

For the foregoing reasons, I respectfully dissent from the majority's decision.

C.A.Fed. (Del.),2009.
In re '318 Patent Infringement Litigation
583 F.3d 1317, 92 U.S.P.Q.2d 1385

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United States Court of Customs and Patent Appeals.
Application of John Nicholson GARDNER, Anthony Maitland Roe and George Lawrence Willey.

Patent Appeal No. 8311.
June 25, 1970.

Proceeding on patent application. The Board of Patent Appeals, serial No. 369,591, affirmed rejection of claims, and applicants appealed. The Court of Customs and Patent Appeals, Rich, Acting C.J., held that claim 3-5 of patent application relating to alleged antidepressant activity in pharmaceutical compounds inadequately disclosed manner of use to alleviate depression.

Affirmed.

West Headnotes

[1] Patents 291 101(6)

291 Patents
291IV Applications and Proceedings Thereon
291k101 Claims
291k101(6) k. Ambiguity, Uncertainty or Indefiniteness. Most Cited Cases

Claims 3-5 of application relating to alleged antidepressant activity in pharmaceutical composition, though broad, were not indefinite.

[2] Patents 291 101(8)

291 Patents
291IV Applications and Proceedings Thereon
291k101 Claims
291k101(8) k. Functions, Advantages or Results of Invention. Most Cited Cases

Claims 3-5 of patent application relating to alleged antidepressant activity in pharmaceutical compounds inadequately disclosed manner of use to alleviate depression. 35 U.S.C.A. § 112.

****786 *1207** Arthur R. Eglington, attorney of record for appellants, George J. Harding, 3rd, Joan S. Keps, Philadelphia, Pa., of counsel.

S. Wm. Cochran, Washington, D.C., for Commissioner of Patents, Leroy B. Randall, Jack Armore, Washington, D.C., of counsel.

Before RICH, Acting Chief Judge, ALMOND, BALDWIN, and LANE, Judges, and FISHER, Chief Judge, Eastern District of Texas, sitting by designation.

RICH, Acting Chief Judge, delivered the opinion of the court:

This appeal is from the decision of the Patent Office Board of Appeals, adhered to on reconsideration, affirming the rejection of claims 1-5, all claims of application serial No. 369,591, filed May 22, 1964, for 'Antidepressant Compositions and Methods of Producing Antidepressant Activity.'

***1208** The Invention

Claims 1 and 2 are directed to pharmaceutical compositions 'having antidepressant activity' and claims 3-5 are directed to a 'method of producing antidepressant activity which comprises internally administering' certain compounds. No claim makes any mention of the subject to which the composition or compound is administered, a fact underlying one of the rejections. Underlying another rejection is the fact that the specification nowhere makes any reference to the subject of the administration of the medication, which the Patent Office herein refers to as the 'host,'[FN1] that is to say, the recipient of the medication.

FN1. Though we doubt the appropriateness of the term 'host' in the context of this case, the medication administered being chemical compounds, we will use it since no one has objected to it. Dorland's Medical Dictionary, 23d Ed. (1955), defines 'host' as 'An animal or plant which harbors or nourishes another organism (parasite).'

The invention here resided in appellants' alleged

discovery of the antidepressant activity in 2-aminomethyl-1, 3-benzodioxole compounds. In view of the nature of the rejections, we need not consider these compounds further. No references are relied on. No objection has been made as to the novelty or utility of the compositions claimed or to the novelty or operativeness of the methods claimed, or to the unobviousness of either, and patentability can be assumed provided the specification and claims comply with the statute.

****787** The Rejections

The rejections before us, as affirmed by the board, are stated in the examiner's Answer as follows:

* * * Claims 3-5 stand rejected as failing to define and particularly point out the invention as required by 35 U.S.C. 112. Claims 3-5 are indefinite in the omission of a host. They are indefinite as to whom the 'administering' is to.

Claims 1-5 stand rejected as being based on a defective specification in that it fails to teach one skilled in the art how to use the invention as required by 35 U.S.C. 112. There is not one specific embodiment of a contemplated host. While dosages are recited on page 6 of the specification and in the claims, they are (1) not related to any host nor (2) are the dosages related to body weight of a host. The question is not one of obviousness, but a failure to 'set forth the best mode contemplated' (35 U.S.C. 112).

The examiner's reference to 'obviousness' was not the obviousness of the claimed invention but was a reply to appellants' argument that, notwithstanding the total absence from the specification of any mention of a host, it would be obvious to those of ordinary skill in the medical art not only that the host would be a human or other animal ***1209** but what the dosage should be. After briefly answering appellants' contentions, the examiner concluded his Answer by saying:

The indefiniteness of the claims in the omission of a host clearly follows from the indefiniteness of the disclosure.

In affirming, the board first found that appellants' specification did not contain a disclosure which satisfies the requirements of the first paragraph of 35 U.S.C. 112 and concluded with this paragraph:

In accordance with the foregoing discussion, the rejection of claims 1 through 5 under the first paragraph of 35 U.S.C. 112 must be sustained. The additional rejection of claims 3, 4, and 5 under the first sentence of the second paragraph of 35 U.S.C. 112 does not require any extended additional discussion. Insofar as the disclosure is incomplete regarding the host, such indefiniteness also attaches to claims 3, 4, and 5, but we are not called upon to rule on the propriety of the method claims if the specification were adequate to satisfy the requirements of the first paragraph of 35 U.S.C. 112.

The decision of the Examiner is affirmed.

The Rejection for Claim Indefiniteness

[1] We will first consider the rejection of claims 3-5 on the ground that they-the claims per se-do not comply with the second paragraph of section 112 because they are indefinite, or, in the examiner's terms, because they do not point out any 'host.'

We are unable to say whether the board affirmed this rejection. It said it was not called upon to rule on the propriety of claims 3-5 if supported by an adequate specification; at the same time it found the specification inadequate and held that its 'indefiniteness,' in failing to specify any host and in not relating dosage to any host, 'attaches' to claims 3-5. Whether or not the board sustained this rejection, we reverse it. We find the claims definite.

While it is true that there is no reference in any claim to a host, it is entirely clear to us that appellants' invention or discovery was in allegedly finding that the group of compounds here involved possess antidepressant activity. This has not been challenged by the Patent Office. It also seems clear to us that pharmaceutical compositions (i.e., one of the compounds in a suitable pharmaceutical carrier) having antidepressant activity would find their primary use as medication for humans with a possibility that they might find some veterinary use in other animals. Appellants say in their arguments-though ****788** not in their application-that while there is no present veterinary use known to them, if one should turn up it would be within their claims. The same observations apply to methods of producing antidepressant activity, as in claims 3-5. We do not find any indefiniteness in any of the claims by reason of their failure to name

***1210** a host. They are merely broad in this respect and cover the composition and the method when administered or applied to any host capable of enjoying the benefits of an antidepressant drug. Breadth is not indefiniteness.

A similar situation obtains with respect to the dosage limitations of the claims. The two composition claims call for dosage units of from about 10 mg. to about 150 mg., and from about 10 mg. to about 100 mg. of the active ingredient, respectively. These ranges are perfectly definite. Claim 3 calls for administering 'an effective amount,' which, though broad, is not indefinite. Where the invention resides in finding the activity rather than in discovering some critical range or the like, we have approved of such broad definitions of quantity or dosage. In re Caldwell, 319 F.2d 254, 50 CCPA 1464 (1963); compare In re Halleck, 422 F.2d 911, 57 CCPA (1970). Claims 4 and 5 call for 'daily dosages' in the ranges 10 to 450 mg. and 10 to 300 mg., respectively. They are enormously wide ranges but there is nothing indefinite about them.

The Rejection for Inadequate Disclosure

[2] We turn now to the other rejection which is based on the inadequacy of the disclosure under the first paragraph of section 112. Appellants say their invention is in the discovery of the antidepressant activity in a group of compounds. They are not claiming the compounds. In effect, by claiming pharmaceutical compositions 'having antidepressant activity' and methods 'of producing antidepressant activity' which consist in administering the compounds, they are claiming in terms of use. It behooves them, therefore, to disclose how to use, as section 112 ordains, 'in such full, clear, concise, and exact terms as to enable any person skilled in the art * * * to * * * use' their invention. Their invention resides in using drugs to alleviate depression. The question is whether they have disclosed how to do this.

The undisputed fact is that the specification nowhere adverts to any recipient of the antidepressant drugs. Neither man nor beast is mentioned- there is no reference to a host. There are four consecutive paragraphs of the specification and one 'example' collectively relating to dosage and administration techniques which can be summarized as saying that the compounds can be put up in all the usual ways, as solids, powders, solutions, and suspensions; in tablets, lozenges, troches, capsules, or ampules; to be administered orally or parenterally; and the carrier may include a time delay material. Whatever the nature of the dosage unit, it may contain anywhere from 10 mg. to ***1211** 150 mg. of the benzodioxole material and the daily dose, whatever the host, may be from 'about 10 mg. to about 450 mg.' With that range, the use of 'about' seems somewhat superfluous.) The Patent Office position is that these generalizations are an insufficient disclosure of how to use and do not comply with the law. Appellants say they are sufficient because anyone in the art would, first of all, assume the host to be an average adult human (at the same time keeping open the possibility of veterinary use), that this is not the first antidepressant drug, and that doctors are 'given sufficient information to properly administer for example any of the four specific dosage unit forms set forth in Example 18.' (That example shows capsules containing 10, 25, 50, and 100 mg. of active ingredient.)

We do not think the disclosure of specific dosage units, ranging all the way from 10 mg. to 150 mg., teaches anyone anything about proper dosage. The only significant dosage disclosure we find is in the statement about daily dosage and ****789** this takes the form of from 10 mg. to 450 mg., a range of from 1 to 45 times. Appellants say:

One of these dosage units may be administered as taught by the specification, until an antidepressant effect is ahchieved especially within the broad daily dosage range of from about 10 mg. to about 450 mg. (Emphasis ours.)

Appellants do not say at what point in the process of administering to a patient, say a 10 mg. capsule, an antidepressant effect may be expected in the course of proceeding at some unspecified intervals toward the possible 45th capsule for the day. Nor do they suggest whether it might be better to start off with a 50 mg. capsule or a 150 mg. capsule.

This uncertainty, particularly when coupled with the total absence of any reference to a host, which, in turn, is coupled with an insistence that, within the claimed invention, the host is not necessarily a human being, amounts to a failure, in our judgment, to comply with the requirements of section 112. As we see it, appellants have in effect said to those skilled in the art:

Here is a new group of compounds in which we have discovered antidepressant activity; you can put them up in convenient dosage units and you can try them out on human patients or animal subjects as you wish and somewhere along the line, from daily doses of from 10 mg. to 450 mg., you will probably get the effect you are after. We consider the range so great as not to be an enabling or how-to-use disclosure as contemplated by the statute. there is not a single specific example or embodiment by way of an illustration of how the invention is to be practiced on any kind of host. We deem it to be in the category on an invitation to experiment in order to determine how to make use of appellants' alleged discovery of the antidepressant activity.

***1212** Appellants argue:

The invention here lies in the well known field of antidepressant drugs for which there is a well known standard drug, imipramine. ('Tofranil'). * * * with imipramine as a standard, a skilled pharmacologist can test an antidepressant composition, such as is claimed here, in rats for an antagonism of reserpine induced ptosis and picrotoxin potentiation, and determine the relative potency of the said antidepressant as compared with imipramine. From this information he can determine the doses to be used in humans, that is to say, if the new antidepressant is twice as active as imipramine in the rat tests, a typical dose in humans would be one-half the normal dose of imipramine. (Emphasis ours.)

In other words, those skilled in the art, by investigations along the above lines, and by a great amount of work, can eventually find out how to use appellants' invention. But our view is that the law requires that the disclosure in the application shall inform them how to use, not how to find out how to use for themselves. The above argument is self-defeating. It demonstrates the inadequacy of the disclosure by saying, in effect: We have detected and disclosed the presence of activity; if you wish to practice our invention, go and find out how to use it.

Appellants rely on two matters outside the disclosure of their specification to support their argument that it is adequate. In response to an initial rejection under 35 U.S.C. § 101 (not now in issue) that utility of the compounds had not been shown, they filed an affidavit of Willey, one of the applicants, reporting on the efficacy of three of their disclosed compounds in the prevention of reserpine-induced ptosis in rats and the potentiation of picrotoxininduced convulsions in rats, as well as toxicity data for two of the three compounds in mice. In the letter submitting the affidavit, in response to the first Office Action, appellants also furnished corresponding data on imipramine ('Tofranil), the known antidepressant drug. The board considered these data and ****790** commented that as a result 'we find greater confusion rather than more enlightenment.' In criticizing the board's analysis of the data, appellants' brief makes the following comments (all emphasis ours):

* * * rats, not being human, do not exhibit mental depression. Further, it is clear from the Willey Affidavit that the rat tests reported are of activities merely indicative of a antidepressant activity in humans and not of antidepressant activity per se. * * *

These tests are relevant only in that reserpine induced ptosis and picrotoxin potentiation in rats have a known correlation with antidepressant activity in man. They are pharmacological tests in nature which are used to find medicinal agents for use in man. Thus Willey was not testing for antidepressant activity as such in rats which, in fact, is an impossibility * * *.

***1213** Here, as discussed above, where tests were of the related activity type, i.e., antagonism of reserpine ptosis and picrotoxin potentiation but not direct tests of antidepressant activity per se, human doses are usually not directly proportional to animal doses. Human doses can only be determined where there is available a standard compound such as imipramine for which there is both a known human dose and known doses from tests in animals such as rats of related activities such as the antagonism of reserpine induced ptosis and picrotoxin potentiation here. In such circumstances, a human dose for a new compound can be determined by obtaining the dose in rats for the related activity of the new compound, establishing an animal dose-activity ratio between the new and old drugs, and then applying the ratio to the human dose of the old drug to obtain the proper dose for the new drug. Thus if the new drug is twice as active in animals as the old drug for a given dose, the human dose for the new drug would most probably be about 50% Of the dose for the old drug.

Now, it is observed that all of this pharmacol-

ogical, posological (dosage) theory is before us only in the form of unsupported statements by appellants' counsel in their brief. There is nothing of the sort in appellants' specification, which contains neither the theory, the animal data, nor the information about the existence or the properties of the alleged standard antidepressant, imipramine. Far from being persuaded by the above arguments that the disclosure is sufficient, we are more firmly convinced thereby that the Patent Office was correct in ruling that it is not. Appellants have not even shown that it was by pursuing such a theory that they arrived at their daily dosage range of from 10 mg. to 450 mg. nor have we been shown any dosage data on imipramine. There has been no disclosure of any 'usual dose' of the claimed compounds or of the antidepressant effect of any specific dose on a human being or other animal.

We hold, therefore, that the rejection of all claims for the reason that the specification fails to comply with the first paragraph of 112 was proper and the decision of the board affirming that rejection is affirmed. Affirmed.

Cust. & Pat.App. 1970.
Application of Gardner
57 C.C.P.A. 1207, 427 F.2d 786, 166 U.S.P.Q. 138

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