United States Court of Appeals for the Federal Circuit

WYETH AND CORDIS CORPORATION,
Plaintiffs/Counterclaim Defendants-Appellants,

v.

ABBOTT LABORATORIES, ABBOTT CARDIOVASCULAR SYSTEMS, INC., AND ABBOTT LABORATORIES, INC.,
Defendants Counterclaimants-Appellees,

AND

MEDTRONIC INC., MEDTRONIC VASCULAR, INC., AND MEDTRONIC USA, INC.,
Defendants/Counterclaimants-Appellees,

AND

BOSTON SCIENTIFIC CORPORATION AND BOSTON SCIENTIFIC SCIMED, INC.,
Defendants/Counterclaimants-Appellees.

2012-1223,-1224

Appeals from the United States District Court for the District of New Jersey in No. 08-CV-0230, Judge Joel A. Pisano.

Decided: June 26, 2013

DAVID T. PRITIKIN, Sidley Austin, LLP, of Chicago, Illinois, argued for plaintiffs/counterclaim defendants-appellants. With him on the brief were CONSTANTINE L. TRELA, JR., WILLIAM H. BAUMAGARTNER, JR., and RUSSELL E. CASS. Of counsel on the brief was BRYAN C. MULDER.

EDWARD A. MAS, II, McAndrews, Held & Malloy, Ltd., of Chicago, Illinois, argued for Defendants/Counterclaimants-Appellees Abbott Laboratories, et al. With him on the brief were SANDRA A. FRANTZEN, STEPHANIE F. SAMZ and KATHLEEN A. DORTON. Of counsel on the brief was SAMUEL F. BAXTER, McKool Smith, P.C., of Dallas, Texas.

MATTHEW M. WOLF, Arnold & Porter, LLP, of Washington, DC, argued for defendants/counterclaimants-appellees Boston Scientific Corporation, et al. With him on the brief were EDWARD HAN and JOHN E. NILSSON.

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

MOORE, *Circuit Judge*.

Wyeth and Cordis Corporation (Wyeth) appeal from the U.S. District Court for the District of New Jersey's grant of summary judgment that claims 1 and 2 of U.S. Patent No. 5,516,781 ('781 patent) and claim 1 of U.S. Patent No. 5,563,146 ('146 patent) are invalid for nonenablement.[1] *Wyeth v. Abbott Labs.*, Nos. 3:08-cv-0230 and -

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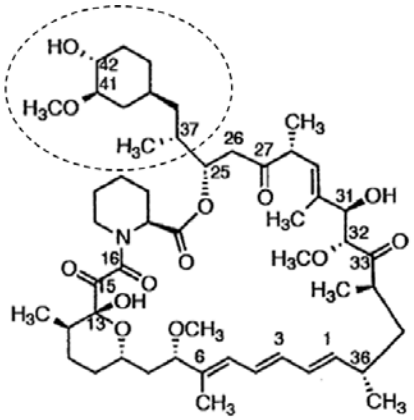
[1] Wyeth also appeals from the court's grant of summary judgment that the claims are invalid for lack of written description based on the "rapamycin" limitation, and invalid for lack of written description and nonenablement based on another limitation. In light of our holding on nonenablement with respect to the "rapamycin" limitation, we need not reach these other issues.

1021, 2012 WL 175023 (D.N.J. Jan. 19, 2012). Because we hold that there is no genuine issue of material fact that the specification does not enable one of ordinary skill to practice the asserted claims without undue experimentation, we *affirm*.

BACKGROUND

The patents-in-suit relate to the use of rapamycin for the treatment and prevention of restenosis, which is the renarrowing of an artery. To open a blocked artery, a physician guides a balloon catheter to the site of accumulated plaque, and then inflates the balloon to crush the plaque. As the balloon inflates, however, it may cause injury to the arterial wall. That vascular injury causes smooth muscle cells to proliferate, which thickens the arterial wall, and, in turn, leads to restenosis.

The claims recite a method of treating or preventing "restenosis in a mammal . . . which comprises administering an antirestenosis effective amount of rapamycin to said mammal." '781 patent, claims 1 and 2; '146 patent, claim 1. In general, "rapamycin" may refer to a class of compounds. While the patents-in-suit use the term "rapamycin," the parties agree that the shared specification discloses only one rapamycin species called sirolimus. Sirolimus is naturally produced by a bacterium called *Streptomyces hygroscopicus*. The structure of sirolimus appears below and includes a substituent group at and beyond the C–37 position (dashed circle) and a macrocyclic triene ring (macrocyclic ring) indicated by the C–1 to C–36 positions.



The parties do not dispute that the effective filing date of both patents is January 9, 1992. At that time, it was known that sirolimus acts in part by binding two proteins at sites within the macrocyclic ring. It was also known that there were four additional compounds with the same macrocyclic ring as sirolimus, but different substituent groups beyond the C–37 position.

The parties also do not dispute that the specification discloses the immunosuppressive and antirestenotic properties of sirolimus. The specification discloses *in vitro* test data indicating that sirolimus inhibits rat smooth muscle cell proliferation. *See* '781 patent col. 5 l. 1–col. 6 l. 2. It also discloses *in vivo* test data indicating that intraperitoneal injection of sirolimus in rats reduced the thickening of the arterial wall following vascular injury. *See id.* col. 6 ll. 39–65, col. 8 l. 17–col. 10 l. 16.

In two separate actions, Wyeth sued the defendants for infringement of the patents-in-suit. The defendants market stent products that elute everolimus and zotarolimus, two drugs that have the same macrocyclic ring as sirolimus but different substituents at the C–42 position. After briefing and a hearing, the district court adopted Wyeth's proposed construction of "rapamycin" as "a compound containing a macrocyclic triene ring structure produced by *Streptomyces hygroscopicus*, having immunosuppressive and anti-restenotic effects." *Wyeth*, 2012 WL 175023, at *3. Based in part on that construction, the

court granted defendants' joint motions for summary judgment of invalidity for nonenablement and lack of written description. *Id.* at *17–18. Wyeth appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

I.

We review a grant of summary judgment under the law of the regional circuit. *Grober v. Mako Prods., Inc.*, 686 F.3d 1335, 1344 (Fed. Cir. 2012). The Third Circuit reviews a grant of summary judgment without deference. *Healy v. New York Life Ins. Co.*, 860 F.2d 1209, 1210 (3d Cir. 1988). Summary judgment is appropriate if "the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." FED. R. CIV. P. 56(a). "The evidence of the nonmovant is to be believed, and all justifiable inferences are to be drawn in his favor." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986).

A patent's specification must describe the invention and "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 . . . to make and use the same." 35 U.S.C. § 112(a) (2012). Claims are not enabled when, at the effective filing date of the patent, one of ordinary skill in the art could not practice their full scope without undue experimentation. *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1380– 81 (Fed. Cir. 2012). Enablement is a question of law based on underlying facts. *Id.*

II.

The central issue on appeal is whether practicing the full scope of the claims requires excessive—and thus undue—experimentation. The district court held that it does. *Wyeth*, 2012 WL 175023, at *17–18. It found that the claims cover any structural analog of sirolimus that exhibits immunosuppressive and antirestenotic effects.

Id. The court also found that, while the specification describes assays to ascertain whether a potential rapamycin compound exhibits the recited functional effects, the only species disclosed is sirolimus. *Id.* In further support of its holding of nonenablement, the court relied on the unpredictability of the chemical arts, the complexity of the invention, and the limited knowledge of treatment of restenosis using sirolimus at the time of the invention. *Id.*

Wyeth argues that the district court ignored evidence that practicing the full scope of the claims would have required only routine experimentation. It contends that the claims do not cover a new genus of compounds, but rather a new use for an existing class of compounds. Wyeth argues that its experts opined that one of ordinary skill would readily know how to practice the full scope of the claims using two steps. First, a skilled artisan could ascertain whether a candidate rapamycin compound has the same macrocyclic ring as sirolimus. Second, a skilled artisan could routinely determine whether a candidate has immunosuppressive and antirestenotic effects using the assays disclosed in the specification.

Regarding the amount of experimentation, Wyeth acknowledges that one of its experts testified that there could be millions of compounds made by varying the substituent groups outside of sirolimus's macrocyclic ring. Wyeth counters that the same expert testified that the number of compounds that would exhibit the recited functional effects would be significantly smaller. According to Wyeth's expert, one of ordinary skill would have understood two relevant facts. First, in order to exhibit the recited functional effects, a compound must be permeable across cell membranes. Second, such permeability typically occurs in compounds having molecular weights below 1,000–1,200 Daltons (sirolimus's molecular weight is approximately 914 Daltons), which further limits the universe of potential rapamycin compounds.

Appellees respond that practicing the full scope of the claims would have required excessive experimentation, even if routine. They argue that the specification is silent on how to structurally modify sirolimus to yield a compound having the recited functional effects. Appellees disagree that one of ordinary skill would have known to select only compounds with a molecular weight below 1,200 Daltons. Even accepting Wyeth's molecular weight argument, however, Appellees respond that there are still tens of thousands of potential compounds that require screening. They emphasize that Wyeth's own witnesses testified that even minor alterations to the sirolimus molecule could impact its immunosuppressive and antirestenotic properties. Appellees argue that one of ordinary skill would thus need, at a minimum, to engage in a laborious iterative process to determine what candidates fall within the claimed genus, and that there is no contrary evidence in the record.

We agree with Appellees and the district court that there is no genuine dispute that practicing the full scope of the claims, measured at the time of filing, would require excessive experimentation. The scope of the claims at issue is broad. Under the district court's unchallenged construction of "rapamycin," the invention is a new method of use of a known compound (sirolimus) *and* any other compounds that meet the construction's structural and functional requirements. We also agree that there is no genuine dispute that the specification's guidance is limited to disclosures of the immunosuppressive and antirestenotic properties of sirolimus and assays to screen for those properties. Wyeth attempts to broaden the background knowledge in the art. It asserts, based in part on expert testing performed in the course of litigation, that the four compounds known to have the same macrocyclic ring as sirolimus at the effective filing date all "*have* immunosuppressive and antirestenotic effects." Appellants' Br. at 14 (emphasis added).

For purposes of summary judgment, we accept as true Wyeth's claims about the state of the art. We also accept Wyeth's expert testimony that one of ordinary skill would have understood that potential rapamycin compounds should have molecular weights below 1,200 Daltons in order to be permeable across cell membranes. We also accept as true that one of ordinary skill could routinely use the assays disclosed in the specification to determine immunosuppressive and antirestenotic effects in candidate compounds. Yet, even accepting Wyeth's assertions, we find no genuine dispute that practicing the full scope of the claims would require more than routine experimentation for two reasons.

First, there is no dispute that, even if potential rapamycin compounds must have a molecular weight below 1,200 Daltons, there are still at least tens of thousands of candidates. The specification is silent about how to structurally modify sirolimus, let alone in a way that would preserve the recited utility. Second, there is no genuine dispute that it would be necessary to first synthesize and then screen *each* candidate compound using the assays disclosed in the specification to determine whether it has immunosuppressive and antirestenotic effects. There is no evidence in the record that any particular substitutions outside of the macrocyclic ring are preferable. Indeed, a Wyeth scientist confirmed the unpredictability of the art and the ensuing need to assay each candidate by testifying that, "until you test [compounds], you really can't tell whether they work or not [*i.e.*, have antirestenotic effects]." J.A. 6929. In sum, there is no genuine dispute that practicing the full scope of the claims would require synthesizing and screening *each* of at least tens of thousands of compounds.

The remaining question is whether having to synthesize and screen each of at least tens of thousands of candidate compounds constitutes undue experimentation. We hold that it does. Undue experimentation is a matter of degree. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247,

1253 (Fed. Cir. 2004) (internal quotation omitted). Even "a considerable amount of experimentation is permissible," as long as it is "merely routine" or the specification "provides a reasonable amount of guidance" regarding the direction of experimentation. *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1360–61 (Fed. Cir. 1998) (internal quotation omitted). Yet, routine experimentation is "not without bounds." *Cephalon, Inc. v. Watson Pharm., Inc.*, 707 F.3d 1330, 1339 (Fed. Cir. 2013).

Our cases have described limits on permissible experimentation in the context of enablement. For example, in *ALZA Corp. v. Andrx Pharmaceuticals, LLC*, we affirmed a judgment of nonenablement where the specification provided "only a starting point, a direction for further research." 603 F.3d 935, 941 (Fed. Cir. 2010) (internal quotation omitted). We concluded that one of ordinary skill "would have been required to engage in an iterative, trial-and-error process to practice the claimed invention even with the help of the . . . specification." *Id.* at 943. In *Cephalon*, although we ultimately reversed a finding of nonenablement, we noted that the defendant had not established that required experimentation "would be excessive, *e.g.*, that it would involve testing for an unreasonable length of time." 707 F.3d at 1339 (citing *White Consol. Indus., Inc. v. Vega Servo-Control, Inc.*, 713 F.2d 788, 791 (Fed. Cir. 1983)). Finally, in *In re Vaeck*, we affirmed the PTO's nonenablement rejection of claims reciting heterologous gene expression in as many as 150 genera of cyanobacteria. 947 F.2d 488, 495–96 (Fed. Cir. 1991). The specification disclosed only nine genera, despite cyanobacteria being a "diverse and relatively poorly understood group of microorganisms," with unpredictable heterologous gene expression. *Id.* at 496.

Here, the specification similarly discloses only a starting point for further iterative research in an unpredictable and poorly understood field. Synthesizing candidate compounds derived from sirolimus could, itself, require a complicated and lengthy series of experiments in synthet-

ic organic chemistry. Even putting the challenges of synthesis aside, one of ordinary skill would need to assay each of at least tens of thousands of candidates. Wyeth's expert conceded that it would take technicians weeks to complete each of these assays. The specification offers no guidance or predictions about particular substitutions that might preserve the immunosuppressive and antirestenotic effects observed in sirolimus. The resulting need to engage in a systematic screening process for each of the many rapamycin candidate compounds is excessive experimentation. We thus hold that there is no genuine dispute that practicing the full scope of the claims, measured at the filing date, required undue experimentation.

We have considered the remainder of Wyeth's arguments and do not find them to be persuasive. Because we find no genuine dispute that the asserted claims are not enabled, we *affirm*.

AFFIRMED