United States Court of Appeals for the Federal Circuit

GLAXOSMITHKLINE LLC
(formerly known as SmithKline Beecham Corporation),
Plaintiff-Appellee,

v.

BANNER PHARMACAPS, INC. AND IMPAX LABORATORIES, INC.,
Defendants-Appellants,

AND

ROXANE LABORATORIES, INC.,
Defendant-Appellant,

AND

MYLAN INC. AND MYLAN PHARMACEUTICALS INC.,
Defendants-Appellants,

AND

WATSON LABORATORIES, INC. FLORIDA,
Defendant-Appellant.

2013-1593, -1594, -1595, -1598

Appeals from the United States District Court for the District of Delaware in Nos. 11-CV-0046, 11-CV-0542 and 11-CV-0789, Judge Richard G. Andrews.

Decided: February 24, 2014

WILLIAM F. LEE, Wilmer Cutler Pickering Hale and Dorr, LLP, of Boston, Massachusetts, argued for plaintiff-appellee. With him on the brief were LISA J. PIROZZOLO and SARAH R. FRAZIER, of Boston, Massachusetts; WILLIAM G. MCELWAIN, THOMAS G. SAUNDERS and MATTHEW GUARNIERI, of Washington, DC; and CHRISTOPHER R. NOYES, of New York, New York.

DEANNE E. MAYNARD, Morrison & Foerster, LLP, of Washington, DC, argued for all defendants-appellants. With her on the brief for defendants-appellants Banner Pharmacaps, Inc., et al., were MARC A. HEARRON, of Washington, DC and PARISA JORJANI, of San Francisco, California. Of counsel on the brief were C. KYLE MUSGROVE and MICHAEL M. SHEN, Haynes and Boone, LLP, of Washington, DC. On the brief for Roxane Laboratories, Inc. were KENNETH G. SCHULER and MARC N. ZUBICK, Latham & Watkins LLP, of Chicago, Illinois; and DARRYLL H. STEENSMA, of San Diego, California. On the brief for Watson Laboratories, Inc. – Florida were GARY E. HOOD and MARK T. DEMING, Polsinelli, PC, of Chicago, Illinois. On the brief for Mylan Inc., et al. were JAMES H. WALLACE, JR., MARK A. PACELLA, and LUCY M. STARK, Wiley Rein, LLP, of Washington, DC.

Before O'MALLEY, WALLACH, and TARANTO, *Circuit Judges.*

TARANTO, *Circuit Judge*.

Plaintiff GlaxoSmithKline LLC ("GSK") sued Banner Pharmacaps, Inc., Impax Laboratories, Inc., Roxane Laboratories, Inc., Mylan Inc., Mylan Pharmaceuticals, Inc., and Watson Laboratories, Inc.–Florida (collectively, "Defendants"). Invoking 35 U.S.C. § 271(e)(2), GSK alleged that drug products containing the molecule dutasteride that Defendants propose to market fall within claims of U.S. Patent No. 5,565,467, which covers dutasteride and its pharmaceutically acceptable solvates. All Defendants stipulated to infringement, which is no longer an issue, but alleged that the asserted claims were invalid for anticipation, lack of utility, lack of enablement, and inadequacy of the written description. After a three-day bench trial, the district court issued an opinion concluding that Defendants did not prove the asserted claims invalid. *GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, No. 11-CV-046, 2013 WL 4082232 (D. Del. Aug. 9, 2013).

Defendants appeal the rejection of their written-description challenge. Their appeal presents only one contention—that "solvate" is not adequately described, whether construed as Defendants urge or as the district court construed it. We affirm, without resolving the claim-construction dispute.

BACKGROUND

This case involves claims to the chemical compound dutasteride and its pharmaceutically acceptable solvates. Claim 1 of the '467 patent, the only independent claim, reads, "17β-N-(2,5-bis(Trifluoromethyl))phenylcarbamoyl-4-aza-5α-androst-1-en-3-one or a pharmaceutically acceptable solvate thereof." '467 patent, col. 16, lines 4-6. The parties agree that dutasteride is the molecule identified before "or a pharmaceutically acceptable solvate thereof." The other asserted claims all recite "[a] pharmaceutical formulation comprising" the "compound of claim 1," subject to further restrictions having no effect on

the issue presented here. *See id.* at col. 16, lines 7-20 (dependent claims 2 through 5).

Dutasteride "is useful in the treatment of androgen responsive diseases." '467 patent, col. 10, lines 19-20. Androgens are a class of hormones—with testosterone "the major circulating androgen"—implicated in a number of diseases, including "benign prostatic hyperplasia, prostate cancer, acne, male pattern baldness and hirsutism." *Id.* at col. 1, lines 18-19, 55-60. In some target tissues, including prostate and skin tissue, testosterone produces certain effects by first being converted to dihydrotestosterone. *See id.* at col. 1, lines 15-25. Dutasteride inhibits the enzymes that catalyze the conversion and thus mitigates some of testosterone's physiological effects, which is sometimes medically desirable. *See id.*

The asserted claims cover not only dutasteride, but also any "pharmaceutically acceptable *solvate thereof*." A "solvate," by definition, is something that originates in a "solution," which is a mixture of two substances: a "solute" dissolved in a "solvent." Salt water is a solution, in which salt is the solute and water the solvent. A solvate is a molecule (a) consisting of a complex made up of solute molecules and solvent molecules (b) resulting from the solution. The parties agree on that much, and also on the proposition that, at least frequently, a solvate complex is "crystalline," a purely structural description referring to the regular, periodic arrangement of the constituent molecules or atoms. The parties disagree about whether "solvate" (in the context of this patent) means *only* such crystalline complexes—a dispute we need not resolve.

Dutasteride has been proven effective in treating benign prostatic hyperplasia, otherwise known as enlargement of the prostate gland. GSK markets Avodart® and Jalyn™, which contain dutasteride and are approved by the Food and Drug Administration to treat symptoms of benign prostatic hyperplasia. Each Defendant filed at

least one Abbreviated New Drug Application under 21 U.S.C. § 355(j), seeking FDA approval to market a generic version of Avodart® or Jalyn™. Each ANDA included a certification under § 355(j)(2)(A) that the '467 patent is invalid, is unenforceable, or would not be infringed by marketing of the proposed generic product. As authorized by 35 U.S.C. § 271(e)(2), GSK responded by suing Defendants for infringement of its '467 patent.

The district court construed "pharmaceutically acceptable" to mean "[s]uitable for use when administered to the recipient thereof as a pharmaceutical." Claim Construction Opinion at 8, *GlaxoSmithKline LLC*, No. 11-CV-046 (D. Del. Nov. 15, 2012). The court also construed "solvate" (of dutasteride), which is the claim term at issue here. GSK and Defendants disagreed about whether the term refers only to crystalline complexes of solute and solvent molecules—that is, of dutasteride (the solute) and some solvent—or, instead, also includes non-crystalline complexes. GSK argued for the broader construction, Defendants for the narrower. The district court acknowledged Defendants' "considerable extrinsic evidence" that, in the pharmaceutical field, "solvate" is limited to crystalline complexes, no matter how created, but it concluded that the specification of this particular patent "direct[ly] contradict[s]" any such narrow usage. *See id.* at 7-8 (relying on '467 patent, col. 3, line 58, through col. 4, line 12). The court construed a "solvate" of dutasteride to mean

> [a] complex formed by dutasteride with a solvent in which dutasteride is reacted or from which it is precipitated or crystallized.

Id. at 4. Despite potential confusion about the meaning of this language, including about what "it" refers to, the parties agree in interpreting the district court's construction to refer to three processes of forming dutasteride solvates—by a reaction of dutasteride with a solvent; by

precipitation of a complex from a solution of dutasteride and a solvent; by crystallization of a complex from a solution of dutasteride and a solvent—with the resulting complex not required to be crystalline.

Defendants stipulated to infringement and have not raised any infringement issue on appeal (not even conditionally, should we reverse the district court's claim construction in deciding the issue they do raise on appeal). The only issue before us is Defendants' invalidity challenge asserting the inadequacy of the written description, a challenge that the district court rejected—along with invalidity challenges asserting anticipation, lack of utility, and lack of an enabling disclosure—after a three-day bench trial held after the stipulation of infringement. Defendants did not dispute that dutasteride is adequately described: it is precisely identified by structure. Instead, they argued that "solvates" of dutasteride, a limitation in all asserted claims, lacked adequate support in the written description. Specifically, Defendants argued that the written description failed to describe the crystalline form of solvate or, more generally, a wide enough range of the solvates included in the district court's construction, which need not be crystalline and could be produced through reaction, precipitation, or crystallization.

Addressing the adequacy of the written description, the district court made various findings, some focused on solvate formation and some on determining which solvates were therapeutically effective. *See GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, No. 11-CV-046, 2013 WL 4082232, at *2-3 (D. Del. Aug. 9, 2013) (findings of fact). It found that dutasteride is "the key structural feature of the solvate" and what "distinguish[es] the '467 [p]atent from the prior art." *Id.* at *2, 8. It found that solvate formation "has been known in the art for over 100 years," that dutasteride is a steroid, that "[s]teroids in particular have been known to be prone to solvate formation since 1983," and that "the universe of solvents

thought to be pharmaceutically acceptable was well-known and relatively small." *Id.* at *2, 6. The court noted that "it [was] difficult or even impossible to *predict* whether a particular solvate form will offer bioavailability, at least prior to the solvate's actual formation," but found that methods to determine the solubility of an already formed solvate "were well-known and routine in the art" and "could be done in less than a week." *Id.* at *6-7 (emphasis added).

The district court concluded that Defendants failed to prove the inadequacy of the written description. According to the district court, "[t]here is no reason why a person skilled in the art would not credit a patentee with possession of a solvate merely because the patentee did not disclose solvates formed by each solvation process," *i.e.*, reaction, precipitation, crystallization. *Id.* at *5. The district court characterized Example 3D—which describes dissolving dutasteride in liquid propylene glycol, *see* '467 patent, col. 15, lines 21-25—as identifying a "reacted" solvate. *Id.* at *7-8. The court found the example, in addition to what was known in the art, "sufficient to meet the written description requirement." *Id.*

The district court rejected not only Defendants' written-description challenge but also their remaining invalidity arguments. In particular, based on extensive findings of fact, the court concluded that the patent enables a person of ordinary skill in the art to make and to use the full range of the claimed molecules. *Id.* at *8-13. Defendants do not appeal that ruling.

Defendants timely appealed, raising only a written-description issue here. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

This appeal presents a single issue: whether, under what is now 35 U.S.C. § 112(a), the written description of

the '467 patent adequately supports the claims to "solvates" of dutasteride. Adequacy of the written description is a question of fact. *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). After a bench trial, we review the district court's findings of fact for clear error. *Pozen Inc. v. Par Pharm., Inc.*, 696 F.3d 1151, 1166 (Fed. Cir. 2012).

Defendants have presented a limited issue. Although noting that the claimed solvates must be "pharmaceutically acceptable," Defendants' brief does not argue that, even if the specification adequately describes "solvates," it inadequately describes the pharmaceutically acceptable ones. There is no such contention, and there is no mention of the "pharmaceutically acceptable" language, in the statement of issues, in the (argument-summarizing) introduction and statement of the case, in the summary of the argument, or in any heading or subheading of the argument section of the brief. The only argument actually developed in the brief is that there is no adequate description of "solvates," whether that term is limited to crystalline structures (as Defendants argue) or covers crystalline and non-crystalline structures, produced through reaction with a solvent or precipitation or crystallization from a solution (as the parties understand the district court's construction). We conclude that Defendants have not properly presented any other contention in this court, especially given the lack of elaboration on the distinct issues that would be raised by a written-description challenge to the phrase "pharmaceutically acceptable."

On the sole issue properly presented, we reject Defendants' challenge. Under either the district court's claim construction or Defendants' claim construction, the claim term "solvate" refers to a molecular complex defined by structure and by the process of creating it, not by what the molecule does. Under the district court's construction, the structure is any complex of dutasteride and solvent,

not necessarily a crystalline complex, resulting from any of three processes: reaction with a solvent or precipitation or crystallization from a solution. Under Defendants' construction, the structure is a complex of dutasteride and a solvent in which the arrangement is crystalline, resulting from crystallization out of a solution. In either event, the written description, which presents materially the same interpretive choice, describes the same class by identifying a particular structure obtained by particular processes. No matter which construction is adopted, the term "solvate" involves no performance property (the claimed compound need not perform an identified function or produce an identified result) and hence raises no issue of insufficient structural, creation-process, or other descriptions to support such a property. In this situation, we affirm the district court's finding that "solvate" is adequately described, without needing to choose between the offered constructions of "solvate."

The Detailed Description provides a description by structure and process of creation that matches the claimed term, whichever construction is preferable. It declares:

> Those skilled in the art of organic chemistry will appreciate that many organic compounds can form complexes with solvents in which they are reacted or from which they are precipitated or crystallized. These complexes are known as "solvates". For example, a complex with water is known as a "hydrate". Solvates of [dutasteride] are within the scope of the invention.
>
> It will also be appreciated by those skilled in organic chemistry that many organic compounds can exist in more than one crystalline form. For example, crystalline form may vary from solvate to solvate. Thus, all crystalline forms of [dutasteride] or the pharmaceutically acceptable solv-

> ates thereof are within the scope of the present invention.

'467 patent, col. 3, line 58, through col. 4, line 12. That language defines the claimed genus by two properties. First, a solvate is a complex of dutasteride molecules and solvent molecules, with dutasteride being, as the district court found, "the key structural component." *GlaxoSmithKline LLC*, 2013 WL 4082232, at *2. Second, the structure is one that is created by an identified process—specifically, by dissolving dutasteride (the solute) in a solvent. Just as they dispute the claim construction, the parties dispute the precise meaning of this passage, including whether the resulting complex must be crystalline and whether it must be produced by just one process or any of three (crystallization only, or any of reaction, precipitation, or crystallization). But under each side's construction and reading of the specification, the description matches the claim, and regardless of which side is right, the description remains entirely based on structure of the compound and its process of creation.

We have no precedent under which this two-condition description, matching the claim scope, would be insufficient. To the contrary, this court has repeatedly "explained that an adequate written description requires a precise definition, such as by *structure*, formula, chemical name, physical properties, or other properties, of species falling within the genus sufficient to distinguish the genus from other materials." *Ariad*, 598 F.3d at 1350 (emphasis added). Describing a complex of dutasteride and solvent molecules is an identification of "structural features commonly possessed by members of the genus that distinguish them from others," allowing one of skill in the art to "visualize or recognize the identity of the members of the genus." *Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997); *cf. Boston Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366-67 (Fed. Cir. 2011) (holding written descrip-

tion inadequate "[g]iven the absence of information regarding structural characteristics of" the claimed genus). The structural identification here is further narrowed by requiring that the structure result from (one or any of three) identified processes. On the (related, though distinct) question of establishing conception, *i.e.*, a definite and permanent idea of the complete and operative invention, we have indicated that it can be enough to identify a compound "by its method of preparation." *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991); *see Fiers v. Revel*, 984 F.2d 1164, 1169 (Fed. Cir. 1993); *id.* at 1171 (written-description analysis referring to earlier conception analysis).

In this case, the claim is no broader in scope than the written description: the above-quoted passage from the written description matches the claim scope (whether they are narrow or broad, as the parties dispute). It is therefore quite different from the claims in *Eli Lilly & Co. v. Teva Pharmaceuticals USA, Inc.*, 619 F.3d 1329, 1344-45 (Fed. Cir. 2010), where the claim covered particle sizes before and after formulation into tablets, but the specification addressed only pre-formulation size. Critically, moreover, the claim term at issue, "solvate," is not functional: to be a "solvate," a compound need not produce a desired result or otherwise perform a certain function. The claim term and its corresponding description, however broad, identify certain structures produced by certain processes. We have not required more for an adequate written description that matches claim scope. And we see no basis for doing so in the present context, where "the concept of solvation . . . has been known in the art for over 100 years" and "[s]teroids in particular [such as dutasteride] have been known to be prone to solvate formation since 1983," *GlaxoSmithKline LLC*, 2013 WL 4082232, at *2, 6, and it is now undisputed that the written description enables a person of skill in the art to make and use the full claimed range of "solvates" of dutasteride.

The claims in this case, not involving functional claim language, do not present the fundamental difficulty presented by the claims in virtually all of the precedents on which Defendants rely. The claims in those cases used functional language: they "cover[ed] any compound later actually invented and determined to fall within the claim's functional boundaries"; such language may "merely recite a description of the problem to be solved [how to produce a desired result] while claiming all solutions to it." *Ariad*, 598 F.3d at 1353. In the field of genetic inventions, our precedents have addressed claims that seek to distinguish members of the claimed genus by the shared performance property of encoding a particular enzyme or other product. *See, e.g., Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1123-24 (Fed. Cir. 2008) (claiming "recombinant plasmids that contain a DNA coding sequence that is broadly defined, and only by its function, *viz.*, encoding DNA polymerase I"); *Eli Lilly*, 119 F.3d at 1562-63 (claiming genetic material capable of "encod[ing] insulin" or "coding for human proinsulin"); *Fiers*, 984 F.2d at 1171 (claiming all DNA "that achieve[s] a result without defining what means will do so"). In other cases, the claimed performance property has been a compound's ability to inhibit the action of a particular protein, *see Ariad*, 598 F.3d at 1340-41; *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 918 (Fed. Cir. 2004), a compound's ability to inhibit a particular medical complication, *see Boston Scientific Corp.*, 647 F.3d at 1364, or an antibody's ability to bind to a particular antigen, *see Noelle v. Lederman*, 355 F.3d 1343, 1349-50 (Fed. Cir. 2004); *In re Alonso*, 545 F.3d 1015, 1018 (Fed. Cir. 2008).

Here, in contrast, under any of the parties' preferred claim constructions, "solvates" of dutasteride are not distinguished by a particular performance property. The claim term does not assert coverage of yet-unidentified ways of achieving a desired result; it does not "attempt to preempt the future before it has arrived." *Fiers*, 984 F.2d

at 1171. This case thus sharply differs from those Defendants invoke. In the circumstances of this case, we have no basis for reversing the district court's finding that the written description conveys to the relevant skilled artisan that "the inventor[s] actually invented the invention claimed." *Ariad*, 598 F.3d at 1351.

CONCLUSION

For the foregoing reasons, we affirm the district court's rejection of Defendants' written-description challenge to the validity of the asserted claims of the '467 patent.

AFFIRMED