United States Court of Appeals for the Federal Circuit

05-1331

PFIZER, INC. and
WARNER-LAMBERT COMPANY, LLC,

Plaintiffs-Appellees,

v.

TEVA PHARMACEUTICALS USA, INC.,

Defendant-Appellant,

RANBAXY PHARMACEUTICALS, INC.
and RANBAXY LABORATORIES LIMITED,

Defendants-Appellants.

DECIDED: November 22, 2005

Before NEWMAN, RADER, and PROST, Circuit Judges.

PROST, Circuit Judge.

Teva Pharmaceuticals USA, Inc. ("Teva") along with Ranbaxy Pharmaceuticals, Inc. and Ranbaxy Laboratories Limited (collectively, "Ranbaxy") appeal from the order of the United States District Court for the District of New Jersey granting a motion for a preliminary injunction filed by Pfizer, Inc. ("Pfizer") and Warner-Lambert Company, L.L.C. ("Warner-Lambert") to prevent Teva and Ranbaxy from infringing United States Patent No. 4,743,450 ("the '450 patent"). Pfizer, Inc. v. Teva Pharms. USA, Inc., No. 05-CV-620 (D.N.J. Mar. 31, 2005) ("Preliminary Injunction Order"); Pfizer, Inc. v. Teva Pharms. USA, Inc., No. 05-CV-620 (D.N.J. Mar. 29, 2005) ("Bench Decision"). At this

preliminary stage in the proceedings, we neither find error in the district court's claim construction, nor do we conclude that the district court abused its discretion in determining that infringement is likely and that the harm and public interest favors enjoining Teva and Ranbaxy. We therefore affirm the grant of the preliminary injunction.

BACKGROUND

I.

The '450 patent relates to pharmaceutical compositions containing angiotensin converting enzyme ("ACE") inhibitors such as quinapril and their methods of manufacture. Quinapril and other ACE inhibitors can be used to treat hypertension, commonly known as high blood pressure. According to the '450 patent, however, many ACE inhibitors including quinapril are susceptible to degradation due to cyclization, hydrolysis, and oxidation. Cyclization occurs when one part of an ACE inhibitor compound reacts with a different part of the same compound to form a degraded, inactive "cyclized" compound. Hydrolysis and oxidation involve reactions with water and oxygen, respectively. Hydrolysis results in a degraded compound, and oxidation causes discoloration.

The '450 patent discloses minimizing cyclization, hydrolysis, and discoloration by using formulations containing a metal-containing stabilizer and a saccharide. According to the '450 patent, the metal-containing stabilizer prevents both cyclization and discoloration, while the saccharide prevents hydrolysis. A contemporaneous report, summarizing the research by the inventors eventually named on the '450 patent, describes how the inventors came to these conclusions. The report explains that the

inventors initially attempted to prevent quinapril drug formulations from decomposing due to cyclization and discoloration. The inventors first suspected that moisture caused these problems and so developed a dry formulation. They chose excipients known to have low moisture content, employing anhydrous lactose as a "filler" and microcrystalline cellulose as a "dry binder." The formulation continued to degrade, however. Eventually the inventors discovered that the two problems, cyclization and discoloration, could be prevented by including magnesium carbonate in the formulations. Use of magnesium carbonate, however, resulted in a new, third problem: hydrolysis. To reduce hydrolysis successfully, the inventors added various proportions of an "inert diluent," lactose. The resulting composition thus eliminated all three problems: cyclization, discoloration, and hydrolysis. Warner-Lambert, which owns the '450 patent, now markets the resulting quinapril formulation as Accupril®.[1]

This appeal involves the '450 patent's independent claims 1 and 16. Claim 1 is a composition claim:

> A pharmaceutical composition which contains:
> (a) a drug component which comprises a suitable amount of an ACE inhibitor which is susceptible to cyclization, hydrolysis, and discoloration,
> (b) a suitable amount of an alkali or alkaline earth metal carbonate to inhibit cyclization and discoloration, and
> (c) a suitable amount of a saccharide to inhibit hydrolysis.

'450 patent, col. 5, l. 52 – col. 6, l. 2. Claim 16 is a process claim:

> A process for stabilizing an ACE inhibitor drug against cyclization which comprises the step of contacting the drug with:

[1] For more background on the development of ACE inhibitors, including Accupril®, see Warner-Lambert Co. v. Teva Pharmaceuticals USA, Inc., 418 F.3d 1326, 1330–33 (Fed. Cir. 2005).

(a) a suitable amount of an alkali or alkaline earth-metal carbonate and,
(b) one or more saccharides.

Id. at col. 6, ll. 54–63.

II.

A.

On January 15, 1999, Teva sought approval from the Food and Drug Administration ("FDA") to market a generic version of Accupril® by filing an Abbreviated New Drug Application ("ANDA") pursuant to the Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act.[2] Because Teva was the first company to file an ANDA for the generic version of Accupril®, Teva was entitled to a 180-day generic market exclusivity period pursuant to 21 U.S.C. § 355(j)(5)(B)(iv). As this court recently explained:

> The 180-day exclusivity period typically begins on the date of the first commercial marketing of the drug by the first applicant. 21 U.S.C. § 355(j)(5)(B)(iv). The original Hatch–Waxman Amendments provided that the commencement of the 180-day exclusivity period could also be triggered by "the date of a decision of a court . . . holding the patent which is the subject of the certification to be invalid or not infringed." Id.

Teva Pharms. USA, Inc. v. Pfizer, Inc., 395 F.3d 1324, 1328 (Fed. Cir. 2005).[3] Along with the ANDA, Teva simultaneously filed a paragraph IV certification pursuant to the

[2] The Hatch-Waxman Amendments were enacted as a part of the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, codified at 21 U.S.C. §§ 355 and 360cc, and 35 U.S.C. §§ 156, 271, 282. Syntex (U.S.A.) L.L.C. v. Apotex, Inc., 407 F.3d 1371, 1376 n.5 (Fed. Cir. 2005).

[3] While in 2003 Congress amended the provisions relating to the 180-day exclusivity period, the new provisions do not apply to Teva's ANDA because it was filed before December 8, 2003. See Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, § 1102(b), 117 Stat. 2066, 2460.

requirements of 21 U.S.C. § 355(j)(2)(A)(vii)(IV), asserting that the '450 patent is invalid under 35 U.S.C. §§ 102 and 103.

On March 2, 1999, Warner-Lambert responded by suing Teva in the District of New Jersey for infringement of the '450 patent under 35 U.S.C. § 271(e)(2)(A). During the course of those proceedings, Teva and Warner-Lambert initially presented diverging claim construction arguments to the district court. In particular, with respect to the claim terms "saccharide" and "saccharides," Teva advocated a construction that would encompass carbohydrates, including polysaccharides and sugars, as well as compounds derived from carbohydrates. For its part, Warner-Lambert simply argued that a "saccharide" is a sugar.[4] Later, however, Teva and Warner-Lambert stipulated to the following claim construction:

> The word "saccharide" in Claims 1 and 16 of the '450 patent means "a sugar, and specifically includes only lower molecular weight carbohydrates, specifically, mono- and disaccharides and their simple derivatives, including such substances as lactose, sucrose, mannitol and sorbitol."

The district court entered this stipulation in an order dated May 7, 2002. The ultimate

[4] In the previous case, Teva and Warner-Lambert disputed the validity of the '450 patent. In the present appeal, the parties only dispute the infringement of the '450 patent. This distinction may explain what will soon become apparent: in this case Teva and Warner-Lambert have each embraced the other's construction of "saccharides" advocated in the previous case.

resolution of that separate case is not at issue in this appeal.[5]

B.

On December 27, 2002, in what would eventually lead to the instant action, Ranbaxy sought FDA approval to market its own generic version of Accupril® by filing its own ANDA and certifying that its product would not infringe the '450 patent. Ranbaxy sent Warner-Lambert a paragraph IV certification letter on April 7, 2003, explaining why Ranbaxy believed its product would not infringe the '450 patent. Ranbaxy's letter indicated that it had adopted and relied upon the construction of "saccharide" Warner-Lambert had previously stipulated to in its case against Teva. Warner-Lambert did not respond to Ranbaxy's letter or sue Ranbaxy within forty-five days of receiving the letter, which would have triggered a thirty-month stay of approval of Ranbaxy's ANDA. See 21 U.S.C. § 355(j)(5)(B)(iii) (2000).

Ranbaxy eventually approached Teva to solicit Teva's assistance in marketing Ranbaxy's product, and on August 26, 2004, the two entered into a Distribution and Supply Agreement. Later, on December 15, 2004, Teva relinquished its potential 180-day generic market exclusivity period, resulting in final FDA approval of Ranbaxy's ANDA. The next day, Teva began marketing Ranbaxy's product.

[5] The district court eventually granted summary judgment against Teva, finding the '450 patent not invalid for lack of enablement and infringed. After a bench trial, the district court also found the '450 patent not unenforceable due to inequitable conduct. This court recently affirmed the finding of no unenforceability for inequitable conduct, but reversed and remanded the case to the district court on the issues of enablement and infringement because the court identified genuine issues of material fact precluding summary judgment. See Warner-Lambert, 418 F.3d at 1348. The court did not, however, have occasion to address the issues presented to it in this appeal.

In response, Pfizer, the corporate parent of Warner-Lambert, and Warner-Lambert (hereinafter, collectively "Warner-Lambert") sued Ranbaxy and Teva (hereinafter, collectively "Ranbaxy") on January 28, 2005 for infringement of the '450 patent. Shortly thereafter, Warner-Lambert filed a motion for a preliminary injunction. The district court granted the motion on March 29, 2005, and issued a detailed explanation of the reasons for granting the motion on March 31, 2005. See Bench Decision; Preliminary Injunction Order.

The court construed "saccharide," as the term is used in claim 1, and "saccharides," as the term is used in claim 16, to include "mono-, di-, tri-, and polysaccharides." In doing so, the court simultaneously rejected both the stipulated construction previously entered in the separate case and Ranbaxy's proposed construction of "sugars, including the lower molecular carbohydrates, specifically mono- and disaccharides." The court found that Warner-Lambert is likely to prove that Ranbaxy's product literally infringes claims 1 and 16 under its construction given that the accused product includes microcrystalline cellulose, a polysaccharide. Because the court rejected Ranbaxy's contention that claim 16 requires Warner-Lambert to show that microcrystalline cellulose inhibits hydrolysis, it concluded that there could be little question that the Ranbaxy formulation literally infringes claim 16. The court noted that, in contrast, claim 1 does require the claimed "saccharide" to inhibit hydrolysis, but credited expert testimony presented by Warner-Lambert as providing a persuasive opinion that microcrystalline cellulose does in fact inhibit hydrolysis. The court went on to determine that even if "saccharides" were construed to mean "sugars," Warner-

Lambert would likely be able to prove infringement of both claims 1 and 16 under the doctrine of equivalents.

After concluding that Warner-Lambert is likely to prove infringement of valid and enforceable claims,[6] the court proceeded to address remaining issues necessary for injunctive relief. It found that Warner-Lambert would suffer irreparable harm due to infringement of the '450 patent. Next, it found that the harm suffered by Ranbaxy in being subject to the injunction would not outweigh the harm Warner-Lambert would suffer in the absence of the injunction. Finally, it determined that granting the injunction was in the public interest since the injunction would further public policy inherent in the patent laws.

The court denied Ranbaxy's motion for a stay of the preliminary injunction. On March 31, 2005, after Warner-Lambert posted a $200,000,000 bond, the preliminary injunction went into effect. Ranbaxy timely appeals the grant of the preliminary injunction. We have jurisdiction to consider the appeal under 28 U.S.C. § 1292(c)(1).

DISCUSSION

Courts have the power to grant injunctions to prevent the violation of patent rights. See 35 U.S.C. § 283 (2000). In considering whether to grant a preliminary injunction, a court must consider whether the patent owner has shown: (1) a reasonable likelihood of success on the merits; (2) the prospect of irreparable harm to the patent owner in the absence of the injunction; (3) that this harm would exceed harm to the alleged infringer when subject to the injunction; and (4) that granting the

[6] The court did not explain the basis for its holding that the claims of the '450 patent are likely valid and enforceable, but Ranbaxy has not appealed the court's decision on these issues.

injunction is in the public interest. Jeneric/Pentron, Inc. v. Dillon Co., 205 F.3d 1377, 1380 (Fed. Cir. 2000); Nutrition 21 v. United States, 930 F.2d 867, 869 (Fed. Cir. 1991).

We review the grant of a preliminary injunction for abuse of discretion. Novo Nordisk of N. Am., Inc. v. Genentech, Inc., 77 F.3d 1364, 1367 (Fed. Cir. 1996). To overturn the grant of a preliminary injunction, we must find that the district court made a clear error of judgment in weighing the relevant factors or based its exercise of discretion on an error of law or on clearly erroneous factual findings. Id.

I.

Ranbaxy first challenges the district court's conclusion that Warner-Lambert is likely to succeed on the merits. To win on its claim of patent infringement, Warner-Lambert must present proof that Ranbaxy infringed a valid and enforceable patent. Nutrition 21, 930 F.2d at 869. Ranbaxy does not appeal the district court's conclusion that the '450 patent is likely valid and enforceable, but instead the district court's finding that infringement is likely. Determining the likelihood of infringement requires two steps, first claim construction and second a comparison of the properly construed claims to the accused product. See Jeneric/Pentron, 205 F.3d at 1380.

A.

We begin with claim construction, a question of law reviewed de novo. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1454–56 (Fed. Cir. 1998) (en banc). When interpreting claims, we inquire into how a person of ordinary skill in the art would have understood claim terms at the time of the invention. Phillips v. AWH Corp., 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). "The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin

claim interpretation." Id. "Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." Id.

Ranbaxy contests the district court's construction of "saccharide" and "saccharides" as those terms are used in independent claims 1 and 16. According to Ranbaxy, the district court should have construed "saccharides" to mean "sugars." In Ranbaxy's view "sugars" would include polysaccharides with up to ten monosaccharide units but would not include polysaccharides, such as microcrystalline cellulose, with more than ten monosaccharide units.

The claim language itself does not support Ranbaxy's proposed construction. "[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms." Id. at 1314. Claim 1 includes "a suitable amount of a saccharide to inhibit hydrolysis," and claim 16 includes "one or more saccharides." It is important to note that the claims do not include the terms "sugar" or "sugars." Neither do the claims distinguish between polysaccharides having ten or less monosaccharide units and polysaccharides having more than ten monosaccharide units.

Ranbaxy argues, however, that the district court erred by not adopting an explicit, narrow definition of "saccharides" set forth in the '450 patent. It points to the following language in the '450 patent: "saccharides (i.e., sugars)." '450 patent, col. 1, ll. 61 – 62. This language is located in a part of the '450 patent discussing what the "invention deals with." Id. at col. 1, l. 44.

This court has previously construed a disputed claim term by referencing use of "i.e." in a patent specification. See Abbott Labs. v. Novopharm Ltd., 323 F.3d 1324,

1327, 1330 (Fed. Cir. 2003). In that case, however, the court did not identify any support in the intrinsic evidence for a construction of the disputed claim term other than the construction linked to "i.e." Id. at 1330. Indeed, the problem with Ranbaxy's argument is that it ignores the fact that the person of ordinary skill in the art is deemed to have read the claim term in the context of the entire patent. Phillips, 415 F.3d at 1313. See also SanDisk Corp. v. Memorex Prods., Inc., 415 F.3d 1278, 1285 (Fed. Cir. 2005) ("The court must always read the claims in view of the full specification." (emphasis added)). "[I]t is necessary to consider the specification as a whole, and to read all portions of the written description, if possible, in a manner that renders the patent internally consistent." Budde v. Harley-Davidson, Inc., 250 F.3d 1369, 1379–80 (Fed. Cir. 2001).

Notably, the '450 patent includes the following discussion in a section entitled "SACCHARIDES":

> The saccharide components to be used in the pharmaceutical products and methods of the invention are substances which are compatible with the alkali or alkaline earth metal-containing stabilizers. Generally, they are substances which do not contain groups which could significantly interfere with the function of either the metal-containing component or the drug component. Mannitol, lactose, and other sugars are preferred. Mixtures are operable.

'450 patent, col. 3, ll. 46–55. By using the label "SACCHARIDES," the patentee clearly intended for this section to address the meaning of the same term.

As a preliminary matter, the first two sentences of this section indicate that a broad construction of "saccharides" may be appropriate. The first sentence explains that "saccharides" are "substances which are compatible with the alkali or alkaline earth metal-containing stabilizers." Id. at col. 3, ll. 49–50. The second explains that

"saccharides" are "substances which do not contain groups which could significantly interfere with the function of either the metal-containing component or the drug component." Id. at col. 3, ll. 51–54. Particularly when compared to the parallel section labeled "EXCIPIENTS," it is clear that these sentences do not affirmatively define what "saccharides" are, but instead negatively define what "saccharides" are not. The section addressing "excipients" similarly states that excipients are "substances which must be compatible with the alkali or alkaline earth metal-containing stabilizers so that it [sic] does not interfere with its [sic] function in the composition." Id. at col. 3, ll. 60–65. Properly understood, then, these sections do not define the exact meaning of "saccharides" and "excipients." Nevertheless, by only indicating what substances should not be considered "saccharides" or "excipients," the patentee has left open a vast array of substances that may be considered to be "saccharides" and "excipients."

Moreover, the section labeled "SACCHARIDES" indicates that the term "saccharides" should not be limited to sugars. The third sentence in this section states that "Mannitol, lactose, and other sugars are preferred." Id. at col. 3, l. 54. Since mannitol is a sugar derivative and not a sugar, were we to accept Ranbaxy's proposed construction of "sugars," we would exclude mannitol from the scope of the '450 patent's use of "saccharides." This would be improper. "A claim construction that excludes a preferred embodiment . . . is 'rarely, if ever, correct.'" SanDisk Corp., 415 F.3d at 1285 (quoting Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1583 (Fed. Cir. 1996)).

Ranbaxy admits that mannitol is not a sugar. It nevertheless argues that the patentee labeled mannitol as a sugar, and that we should respect the patentees'

decision to do so. Thus, according to Ranbaxy, "Mannitol, lactose, and other sugars are preferred" is, for the purpose of the patent, a list of like ingredients, "sugars."

We are not convinced that one of ordinary skill in the art would understand the patentee to have classified mannitol as a sugar in this sentence. As the district court found and Ranbaxy does not dispute on appeal, mannitol is not actually a sugar. On the other hand, lactose is a sugar. The reference to "other sugars" therefore appears to relate to the disclosure of lactose only. In short, the reference to "other sugars" does not mean that mannitol is a sugar or should be considered to be a sugar for purposes of the '450 patent.

Even if we concluded that Ranbaxy's reading of "Mannitol, lactose, and other sugars are preferred" is correct and that mannitol, a sugar derivative, should be considered to be a sugar for the purpose of the '450 patent, this sentence would only identify sugars as being preferred embodiments of "saccharides." We hesitate to adopt a construction of "saccharides" that would be limited to disclosed preferred embodiments. See Playtex Prods., Inc. v. Procter & Gamble Co., 400 F.3d 901, 907–08 (Fed. Cir. 2005). Indeed, identifying sugars as preferred saccharides seems to indicate that there is a broader, albeit less preferred class of substances that are still "saccharides."

Extrinsic evidence in the form of technical dictionaries, treatises, and expert testimony supports the conclusion drawn from the '450 patent that one of skill in the art would understand "saccharides" to encompass more than sugars. The district court reviewed the extrinsic evidence presented by the parties and found that one of skill in the art would understand "saccharides" to include polysaccharides. Ranbaxy, however,

points to specific examples of references and testimony that allegedly support its view that "saccharides" means sugars.

Based on our review of the preliminary record, we do not disagree with the district court's conclusion that a person of ordinary skill in the art would understand "saccharides" to encompass polysaccharides. The district court weighed the disclosures of the competing references and testimony and concluded that the "general view" is that the saccharides include polysaccharides. Contrary to Ranbaxy's assertions, the district court did not err by referencing dictionary definitions of "saccharides." As this court has held, judges may "'rely on dictionary definitions when construing claim terms, so long as the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents.'" Phillips, 415 F.3d at 1322–23 (quoting Vitronics, 90 F.3d at 1584 n.6). And as discussed above, when read in the context of the entire '450 patent, the reference to "saccharides (i.e., sugars)" does not constitute a definition of "saccharides."

Furthermore, the district court's conclusion that the "general view" is that the group of substances called saccharides includes polysaccharides appears to be well supported. As Warner-Lambert notes, many of the references cited by Ranbaxy do not actually address the scope of the term "saccharides." Rather, they clarify that sugars and polysaccharides are both subclasses of the larger class of substances called carbohydrates. For example, one reference submitted by Ranbaxy states that "carbohydrates" include both sugars and polysaccharides. As the district court noted, however, even that reference stated that "[t]he carbohydrates are sometimes referred to as the saccharides." Edward Staunton West et al., Textbook of Biochemistry 174

(MacMillan 4th ed. 1966) (1951).

Ranbaxy faults the district court for relying on this text in view of its use of the word "sometimes." Ranbaxy also alleges that to reach its conclusion the district court was forced to ignore the next sentence in the reference, which explains that "'saccharide' comes from the Greek word sakcharon, meaning sugar." Id.

We do not believe that the district court erred in its analysis. First, evidence that "saccharides" is sometimes used to refer to "carbohydrates" does support the conclusion that the '450 patent in particular may be understood to have used "saccharides" to mean "carbohydrates." Thus, reliance on this disclosure to support the district court's construction is not improper. Second, understanding the historical origin of the term "saccharides" does not exactly answer the question of how one of ordinary skill in the art would interpret the term on the filing date of the '450 patent. "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." Phillips, 415 F.3d at 1313. We therefore do not fault the district court for not considering the historical origin of "saccharides" to be dispositive of the term's meaning to those skilled in the art.

To support its proposed construction, Ranbaxy also points us to the construction of "saccharides" previously agreed upon by two of the parties to this case in separate litigation:

> The word "saccharide" in Claims 1 and 16 of the '450 patent means "a sugar, and specifically includes only lower weight carbohydrates, specifically, mono- and disaccharides and their simple derivatives, including such substances as lactose, sucrose, mannitol and sorbitol."

Ranbaxy asks us to adopt this construction in this appeal.

Ranbaxy has not identified any legal doctrines that would compel us to adopt the stipulated construction. And to the extent Ranbaxy's argument addresses issue preclusion, we conclude that issue preclusion does not apply in this case. The district court noted that the stipulation presented to the court in the earlier litigation specifically stated that it was for the purposes of that litigation only. Bench Decision, slip op. at 13. Because Ranbaxy does not dispute this finding, issue preclusion cannot apply to this case. "[T]he scope of a consent decree must be discerned within its four corners" and the conditions upon which a party has consented to waive its right to litigate particular issues "must be respected." United States v. Armour & Co., 402 U.S. 673, 682 (1971). See also In re Graham, 973 F.2d 1089, 1097 (3rd Cir. 1992) (noting that the Third Circuit defers to the intent of parties concerning the preclusive effect of agreed facts or claims in consent decrees and stipulations). While we do not fault Ranbaxy to the extent it may have adopted or relied upon the stipulated construction of "saccharide," that stipulation does not define the scope of the invention claimed in the '450 patent for purposes of this case.

Ranbaxy additionally contends that the district court's claim construction would render the claims invalid for lack of enablement under 35 U.S.C. § 112, ¶ 1. In Phillips, this court stated:

> While we have acknowledged the maxim that claims should be construed to preserve their validity, we have not applied that principle broadly, and we have certainly not endorsed a regime in which validity analysis is a regular component of claim construction. Instead, we have limited the maxim to cases in which the court concludes, after applying all the available tools of claim construction, that the claim is still ambiguous. In such cases, we have looked to whether it is reasonable to infer that the PTO would not have issued an invalid patent, and that the ambiguity in the claim language should therefore be resolved in a manner that would preserve the patent's validity.

415 F.3d at 1327 (citations and quotation marks omitted). Both Ranbaxy and Warner-Lambert were able to find at least some extrinsic evidence supporting their proposed constructions of "saccharides." Nevertheless, Ranbaxy has not presented sufficient evidence for us reasonably to infer that, unless "saccharides" means "sugars" or at least does not encompass polysaccharides, claim 1 and 16 would have been considered by the Patent and Trademark Office ("PTO") to be invalid. We therefore decline to apply the maxim in this case.

For the reasons discussed, we conclude that the district court did not err in construing "saccharides" to include polysaccharides.

B.

We next consider whether the district court clearly erred in its comparison of the properly construed claims to the accused products and methods. To prove infringement, a patentee must show that an accused product or method meets every claim limitation either literally or under the doctrine of equivalents. See Dynacore Holdings Corp. v. U.S. Philips Corp., 363 F.3d 1263, 1273 (Fed. Cir. 2004).

1.

The district court did not clearly err in determining that Warner-Lambert is likely to prevail in its charge that Ranbaxy literally infringes claim 16. Ranbaxy conceded in the preliminary injunction hearing that its formulation "absolutely" literally infringes claim 16 if "saccharides" is construed to include polysaccharides. Given that concession and the fact that we have construed "saccharides" to include polysaccharides, we cannot help but conclude that the district court was on solid ground in finding that it is likely that Ranbaxy literally infringes claim 16.

The district court also did not clearly err in determining that Warner-Lambert is likely to prevail in its charge that Ranbaxy literally infringes claim 1. In contrast to claim 16, claim 1 specifically requires that a saccharide "inhibit hydrolysis." In finding that the microcrystalline cellulose in Ranbaxy's formulation likely inhibits hydrolysis, the district court credited the testimony of one of Warner-Lambert's experts, Dr. Brenner, stating:

> Significantly, Ranbaxy has offered no evidence countering Dr. Brenner's opinions concerning the manner in which hydrolysis is inhibited in its formulations. This is information peculiarly within Ranbaxy's possession. Hydrolysis must be inhibited in its formulation; otherwise it could not have submitted its ANDA to the FDA. Dr. Brenner gives a persuasive opinion that it is the saccharide microcrystalline cellulose that has this effect. Ranbaxy offers nothing but speculation to counter his opinion.

Bench Decision, slip op. at 19.

Ranbaxy's challenges to the district court's finding are easily rejected. Ranbaxy first points out that Dr. Brenner did not test Ranbaxy's product but instead relied upon tests conducted during previous cases involving two different products. But it is particularly appropriate at the preliminary injunction stage not to set a hard and fast rule that infringement can only be shown through quantitative testing of an accused product. Cf. Water Techs. Corp. v. Calco, Ltd., 850 F.2d 660, 667 (Fed. Cir. 1988) (refusing to overturn a finding of infringement based on the lack of quantitative testing to determine the exact composition of the accused product). Ranbaxy also contends that the district court improperly shifted to Ranbaxy the burden of showing that microcrystalline cellulose does not inhibit hydrolysis. The district court, however, did no such thing. The district court weighed the evidence submitted by the parties. In doing so, the court was at least entitled, and probably even required, to consider the lack of evidence submitted by Ranbaxy.

2.

Because we have held that the district court did not err in construing "saccharides" to include polysaccharides or abuse its discretion in concluding that literal infringement is likely, we need not respond to Ranbaxy's contention that the district court erred in its application of the doctrine of equivalents. We recognize, however, that the district court's claim construction, as well as our claim construction, is based on a record developed at the preliminary injunction stage of this case. We also recognize that "[d]istrict courts may engage in rolling claim construction, in which the court revisits and alters its interpretation of the claim terms as its understanding of the technology evolves." Jack Guttman, Inc. v. Kopykake Enters., Inc., 302 F.3d 1352, 1361 (Fed. Cir. 2002). Indeed, a conclusion of law such as claim construction is subject to change upon the development of the record after a district court's decision on a motion for preliminary injunction. Id. (citing Purdue Pharma L.P. v. Boehringer Ingelheim GmbH, 237 F.3d 1359, 1363 (Fed. Cir. 2001)). Thus, we find it prudent to address Ranbaxy's contention that the district court wrongly concluded that infringement under the doctrine of equivalents is likely.

The district court did not clearly err in holding in the alternative that, even if "saccharides" were construed to include sugars but not polysaccharides, Ranbaxy likely infringes claims 1 and 16 under the doctrine of equivalents. Ranbaxy argues that the district court erred in its analysis of claim 16 by not assigning any function to "saccharides" for purposes of equivalency. It argues that the court should have assigned to "saccharides" the function of inhibiting hydrolysis. Thus, in Ranbaxy's view the district court clearly erred in its analysis of both claim 1 and claim 16 because the

evidence does not show that it is likely that microcrystalline cellulose inhibits hydrolysis. As discussed above with regard to literal infringement of claim 1, however, the district court did not clearly err in finding to the contrary. It was perfectly appropriate for the district court to credit the testimony of Warner-Lambert's expert, Dr. Brenner, explaining that microcrystalline cellulose does in fact inhibit hydrolysis.

Ranbaxy also contends that as a matter of law microcrystalline cellulose cannot be an equivalent of a "saccharide" because the patentee dedicated microcrystalline cellulose to the public by disclosing but not claiming its use in the '450 patent. One alleged disclosure is a listing of "modified cellulose derivatives" as an example of a "disintegrating agent." '450 patent, col. 4, ll. 3–7. Another is Example C in the '450 patent, which discloses a prior art composition containing microcrystalline cellulose. Id. at col. 5, ll. 15–30. The district court concluded that the patentee did not dedicate use of microcrystalline cellulose to the public because "[o]nly those compounds or articles that are clearly identified as alternatives to what is actually claimed are subject to the bar" against recapturing disclaimed subject matter using the doctrine of equivalents. Bench Decision, slip op. at 24. According to Ranbaxy, however, our precedent is not so restrictive. Ranbaxy argues we have not required that the patent expressly disclose the subject matter left unclaimed as an alternative to the claim limitation at issue. Application of the disclosure-dedication rule is a question of law subject to de novo review. See Toro Co. v. White Consol. Indus., Inc., 383 F.3d 1326, 1331 (Fed. Cir. 2004).

Ranbaxy is correct to the extent it points out that our precedent addressing the disclosure-dedication rule appears to deal only with patents in which subject matter is

disclosed as an alternative to the relevant claim limitation. See, e.g., Johnson & Johnston Assocs. Inc. v. R.E. Serv. Co., 285 F.3d 1046 (Fed. Cir. 2002) (en banc); PSC Computer Prods., Inc. v. Foxconn Int'l, Inc., 355 F.3d 1353 (Fed. Cir. 2004); Toro, 383 F.3d at 1326. For example, in PSC Computer Products this court answered the question of how specific a disclosure in a written description must be to dedicate matter to the public:

> We hold that if one of ordinary skill in the art can understand the unclaimed disclosed teaching upon reading the written description, the alternative matter disclosed has been dedicated to the public. This "disclosure-dedication" rule does not mean that any generic reference in a written specification necessarily dedicates all members of that particular genus to the public. The disclosure must be of such specificity that one of ordinary skill in the art could identify the subject matter that had been disclosed and not claimed.

355 F.3d at 1360. This court found that the generic disclosure of a class of unclaimed alternatives, "other resilient materials," does not necessarily dedicate all members of that class to the public. On the other hand, the court did find specifically disclosed but unclaimed alternatives, "molded plastic parts," to have been dedicated to the public when only metal parts were claimed. Id. The court reasoned that "[a] reader of ordinary skill in the art could reasonably conclude from . . . language in the written description that plastic clip parts could be substituted for metal clip parts." Id.

This case presents a slightly different scenario: generic and specific disclosures of subject matter, but subject matter that is not specifically identified as being an alternative to a claim limitation. Nevertheless, in PSC Computer Products the driving force behind the court's holding was the public notice function of patents. Id. And in our view, the public notice function of patents suggests that before unclaimed subject matter

is deemed to have been dedicated to the public, that unclaimed subject matter must have been identified by the patentee as an alternative to a claim limitation.

In this case, even if "saccharides" were construed to mean "sugars," Ranbaxy has not pointed to parts of the '450 patent where the inventors identify microcrystalline cellulose as an unclaimed alternative that would function as a "saccharide" preventing hydrolysis. As the district court found, modified cellulose derivatives are only discussed as examples of a "disintegrating agent," one of various "optional excipients." '450 patent, col. 3, l. 60 – col. 4, l. 10. Furthermore, while Example C identifies microcrystalline cellulose as an ingredient in a particular formulation, we are not convinced that one of ordinary skill in the art would come to the conclusion that the inventors have identified microcrystalline cellulose in that formulation as an alternative to a "saccharide" that prevents hydrolysis. The '450 patent states that Example C discloses a "standard," prior art formulation "without the addition of a stabilizer of the present invention." Id. at col. 5, ll. 14–17. Indeed, the ingredient list does not include magnesium carbonate, and the '450 patent does not contend that Example C prevents cyclization. See id. at col. 5, ll. 20–28, 46–55. Instead, Example C appears to correspond to the first, unsuccessful formulation devised by the inventors in an attempt to prevent cyclization: the ingredient list includes both anhydrous lactose and microcrystalline cellulose. Id. at col. 5, ll. 20–23. As discussed above, not until magnesium carbonate was introduced into formulations did hydrolysis become a major problem. Thus, a saccharide was not needed to prevent hydrolysis in Example C. In short, Example C does not appear to relate to the claimed invention. For these

reasons, we hold that the patentee did not dedicate to the public the use of microcrystalline cellulose as a "saccharide" to prevent hydrolysis.

Ranbaxy next contends that the all limitations rule precludes application of the doctrine of equivalents. Ranbaxy argues that Warner-Lambert cannot now assert that microcrystalline cellulose is an equivalent to the claimed "saccharide" because to do so would impermissibly vitiate the "saccharide" and "saccharides" limitations. Like the disclosure-dedication rule, application of the all limitations rule is a question of law subject to de novo review. See Seachange Int'l, Inc. v. C-COR Inc., 413 F.3d 1361, 1378 (Fed. Cir. 2005).

The all limitations rule "provides that the doctrine of equivalents does not apply if applying the doctrine would vitiate an entire claim limitation." Asyst Techs., Inc. v. Emtrak, Inc., 402 F.3d 1188, 1195 (Fed. Cir. 2005). We have explained:

> There is no set formula for determining whether a finding of equivalence would vitiate a claim limitation, and thereby violate the all limitations rule. Rather, courts must consider the totality of the circumstances of each case and determine whether the alleged equivalent can be fairly characterized as an insubstantial change from the claimed subject matter without rendering the pertinent limitation meaningless.

Freedman Seating Co. v. Am. Seating Co., 420 F.3d 1350, 1359 (Fed. Cir. 2005).

Based on the totality of the circumstances, even if "saccharides" were construed to mean "sugars," we conclude that microcrystalline cellulose can be fairly characterized as an insubstantial change from the claimed subject matter without rendering the "saccharide" limitations meaningless. As discussed above, the district court pointed to evidence that microcrystalline cellulose, like sugars, performs the function of inhibiting hydrolysis. Moreover, microcrystalline cellulose, a polysaccharide, is a substance having many monosaccharide units, which are the building blocks of sugars. These

similarities convince us that microcrystalline cellulose can be fairly characterized as an insubstantial change when compared to "sugars." Moreover, such a characterization would not render the claim limitations meaningless. Thus, the all limitations rule does not preclude application of the doctrine of equivalents in this case.

For the reasons discussed, we conclude that the district court did not clearly err in its comparison of the claims to the accused products and methods based on the preliminary record.

II.

Ranbaxy maintains that the district court clearly erred in its consideration of the prospect of irreparable harm to the patent owner in the absence of the injunction. The district court presumed irreparable harm based on its finding that Warner-Lambert is likely to succeed on the merits, citing Purdue Pharma L.P., 237 F.3d at 1363. The court also analyzed the potential for harm to Warner-Lambert and found that Ranbaxy's sales of its generic product would cause substantial harm to Warner-Lambert and loss of the statutory right to exclude Ranbaxy for the remaining life of the '450 patent, which expires in August 2007. The court also noted that Warner-Lambert has fought Teva vigorously to protect its rights under the '450 patent.

According to Ranbaxy, the court should not have presumed irreparable harm because Ranbaxy's product does not infringe any claim of the '450 patent. Ranbaxy cites Reebok International Ltd. v. J. Baker, Inc., 32 F.3d 1552, 1558–59 (Fed. Cir. 1994), and Illinois Tool Works, Inc. v. Grip-Pak, Inc., 906 F.2d 679, 683 (Fed. Cir. 1990), for the proposition that the loss of the statutory right to exclude alone does not constitute irreparable harm. Ranbaxy further argues that the district court failed to

consider evidence that Warner-Lambert does not currently enjoy market exclusivity. For example, Ranbaxy points out that various competitors have begun selling competing generic products. Ranbaxy also argues that Warner-Lambert's grant of a license under the '450 patent shows that any injury suffered by Warner-Lambert would be compensable in monetary damages. Ranbaxy additionally claims that Warner-Lambert should not be excused for its decision not to bring suit within forty-five days of receiving Ranbaxy's paragraph IV certification letter dated April 7, 2003, which would have triggered the thirty-month stay of FDA approval of Ranbaxy's ANDA, see 21 U.S.C. § 355(j)(5)(B) (2000); 35 U.S.C. § 271(e)(2)(A) (2000).

Warner-Lambert responds by pointing to evidence that shows that sales of Ranbaxy's product dwarf the sales of other competitors' generic products. And while Warner-Lambert admits that it has granted a license to the '450 patent, it clarifies that the license is exclusive and limited to moexipril products and not quinapril products such as Accupril®. Warner-Lambert further explains that it did not sue Ranbaxy within forty-five days of receiving Ranbaxy's paragraph IV certification letter because Teva, as the first ANDA filer, had a potential 180-day exclusivity period, which precluded FDA approval of any later ANDA.

The district court did not abuse its discretion by presuming irreparable harm. We have consistently held that a district court should presume that a patent owner will be irreparably harmed when, as here, a patent owner establishes a strong showing of likely infringement of a valid and enforceable patent. See, e.g., Jack Guttman, Inc., 302 F.3d at 1356; Purdue Pharma, 237 F.3d at 1363; Datascope Corp. v. Kontron Inc., 786 F.2d 398, 400 (Fed. Cir. 1986).

The district court also did not abuse its discretion in finding that Ranbaxy failed to rebut the presumption of irreparable harm. In Polymer Technologies, Inc. v. Bridwell, this court explained that because the very nature of a patent provides the right to exclude, infringement of a valid patent inherently causes irreparable harm in the absence of exceptions such as a finding that future infringement is no longer likely, that the patentee is willing to forgo its right to exclude by licensing the patent, or that the patentee had delayed in bringing suit. 103 F.3d 970, 975 (Fed. Cir. 1996). And when the presumption of irreparable harm attaches, the burden is on the likely infringer to produce evidence sufficient to establish that the patent owner would not be irreparably harmed by an erroneous denial of a preliminary injunction. Id. at 974. The court explained that in Reebok "the presumption of irreparable harm was rebutted by evidence that neither the patentee nor the alleged infringer would be continuing to manufacture or sell the devices covered by the patent (except for a small amount of residual stock)." Id. at 975. The court also explained that in Illinois Tool Works "we held that potential lost sales alone could not demonstrate 'manifest irreparable harm' in light of other evidence that the movant had granted a non-exclusive license to a non-party." Id. In contrast to those cases, here, it is clear that neither party anticipates voluntarily ceasing the sale of products covered by the '450 patent, and there is no evidence that Warner-Lambert intends to engage in non-exclusive licensing of its rights under the '450 patent.

While Warner-Lambert admits that two competitors remain in the marketplace, "[t]he fact that other infringers may be in the marketplace does not negate irreparable harm. A patentee does not have to sue all infringers at once. Picking off one infringer

at a time is not inconsistent with being irreparably harmed." Id. Neither is first targeting infringers whose sales dwarf the sales of other infringers.

The fact that Warner-Lambert has granted a narrow, exclusive license under the '450 patent also does not require that the district court find that any harm would not be irreparable. The grant of such a license is simply not a sufficient basis to overturn the district court's conclusion that Warner-Lambert did not engage in a pattern of licensing destroying market exclusivity. See id. at 974 (noting that engagement in a pattern of granting licenses under a patent evidences the reasonableness of the ability to recompense invasion of patent rights using a royalty rather than an injunction).

The district court also did not abuse its discretion by not faulting Warner-Lambert for its decision not to bring suit within forty-five days of receiving Ranbaxy's paragraph IV certification letter. Ranbaxy is correct to point out that evidence that a patent owner unduly delays in bringing suit against an alleged infringer negates the idea of irreparability. See id. And Ranbaxy is also correct that the relevant statutory provisions would have triggered the thirty-month stay of FDA approval of Ranbaxy's ANDA had Warner-Lambert sued. But there is no requirement that a patent owner take advantage of the statutory carrot of a thirty-month stay, and certainly no statutory stick for choosing not to. Moreover, Teva, as the first party to file an ANDA, held exclusive generic rights. There was therefore no immediate need for Warner-Lambert to sue Ranbaxy. And the fact that Warner-Lambert filed suit against Ranbaxy within two months of the launch of Ranbaxy's quinapril formulation supports the district court's rejection of the idea that Warner-Lambert unduly delayed in bringing suit against Ranbaxy. Thus, the district

court did not clearly err or otherwise abuse its discretion in determining that Ranbaxy did not meet its burden of rebutting the presumption of irreparable harm.

For the reasons discussed, we conclude that the district court did not abuse its discretion in its analysis of the harm to Warner-Lambert.

III.

Ranbaxy next challenges the district court's conclusion that the harm to Warner-Lambert in the absence of an injunction would exceed the harm to Ranbaxy when Ranbaxy is subject to the injunction. The district court held that the fact that Ranbaxy "built up its manufacturing facility in India and prepared to market [its] product was simply a risk it took with eyes open to the consequences." Bench Decision, slip op. at 26. Ranbaxy responds by arguing that, in contrast to Warner-Lambert, it is facing real and immediate irreparable harm since the preliminary injunction has forced it to remove its product from the market, thereby causing Ranbaxy to lose market share and customer relationships.

The district court did not abuse its discretion in finding that the harm favors enjoining Ranbaxy. Simply put, an alleged infringer's loss of market share and customer relationships, without more, does not rise to the level necessary to overcome the loss of exclusivity experienced by a patent owner due to infringing conduct.

IV.

Ranbaxy finally argues that the district court erred in assessing the public interest. Ranbaxy contends that the public interest favors denying the preliminary injunction because the statutory framework under which Ranbaxy filed its ANDA makes low cost generic drugs available to the public through increased competition. The

district court rejected Ranbaxy's argument by pointing out that a preliminary injunction that enforces a valid patent against an infringer "does no more than further public policy inherent in the patent laws designed to encourage useful inventions by rewarding the inventor with a limited period of market exclusivity." Id.

The district court did not abuse its discretion in rejecting Ranbaxy's argument. "[S]elling a lower priced product does not justify infringing a patent." Payless Shoesource, Inc. v. Reebok Int'l Ltd., 998 F.2d 985, 991 (Fed. Cir. 1993). And while the statutory framework under which Ranbaxy filed its ANDA does seek to make low cost generic drugs available to the public, it does not do so by entirely eliminating the exclusionary rights conveyed by pharmaceutical patents. Nor does the statutory framework encourage or excuse infringement of valid pharmaceutical patents.

CONCLUSION

We affirm the grant of the preliminary injunction. Based on the preliminary record, the district court's claim construction was not erroneous; the district court did not abuse its discretion when it determined that Ranbaxy likely infringes the '450 patent either literally or under the doctrine of equivalents; and the district court did not abuse its discretion when it found that the harm and public interest favors enjoining Ranbaxy.

COSTS

Each party shall bear its own costs.

AFFIRMED