United States Court of Appeals for the Federal Circuit

AMGEN INC., AMGEN MANUFACTURING LTD.,
Plaintiffs-Appellants

v.

COHERUS BIOSCIENCES INC.,
Defendant-Appellee

2018-1993

Appeal from the United States District Court for the District of Delaware in No. 1:17-cv-00546-LPS, Chief Judge Leonard P. Stark.

Decided: July 29, 2019

NICHOLAS P. GROOMBRIDGE, Paul, Weiss, Rifkind, Wharton & Garrison LLP, New York, NY, argued for plaintiffs-appellants. Also represented by JENNIFER GORDON, GOLDA LAI, PETER SANDEL, JACOB WHITT, JENNIFER H. WU; LOIS M. KWASIGROCH, KIMBERLIN L. MORLEY, WENDY A. WHITEFORD, Amgen Inc., Thousand Oaks, CA.

ADAM G. UNIKOWSKY, Jenner & Block LLP, Washington, DC, argued for defendant-appellee. Also represented by BRADFORD PETER LYERLA, AARON A. BARLOW, LOUIS FOGEL, SUSAN O'BRIEN, Chicago, IL.

Before REYNA, HUGHES, and STOLL, *Circuit Judges*.

STOLL, *Circuit Judge*.

Amgen Inc. and Amgen Manufacturing Ltd. (collectively, "Amgen") sued Coherus BioSciences Inc. for patent infringement in the District of Delaware. The district court dismissed Amgen's complaint for failure to state a claim, and Amgen appeals. Because prosecution history estoppel bars Amgen from succeeding on its infringement claim under the doctrine of equivalents, we affirm the order of the district court.

BACKGROUND

I

Recombinant therapeutic proteins are a class of biologic medicines that are manufactured inside living cells. Before a protein can be therapeutically useful, it must first be purified from contaminants. Amgen's U.S Patent No. 8,273,707 claims methods of purifying proteins using hydrophobic interaction chromatography ("HIC"). A HIC column contains a solid, hydrophobic matrix and "is used to separate proteins on the basis of hydrophobic interactions between the hydrophobic moieties of the protein and insoluble, immobilized hydrophobic groups on the matrix." '707 patent col. 1 ll. 36–39. In a HIC purification, a buffered salt solution containing the desired protein and associated impurities is first poured onto a HIC column. *Id.* at col. 1 ll. 40–41. This is known as the "loading" step. The salt in the buffer exposes the hydrophobic regions of the protein and causes them to adsorb (*i.e.*, attach) onto the hydrophobic groups on the column matrix. *See id.* at col. 1 ll. 41–44. The impurities are then washed out of the column with a buffered salt solution while the desired protein remains attached to the matrix. *See id.* at col. 4 ll. 27–29. Finally, molecules of the desired protein are detached (or "eluted") by pouring a buffer solution with a lower salt concentration through the column. *See id.* at col. 1 ll. 44–49.

"Usually, a decreasing salt gradient is used to elute proteins from a column. As the ionic strength decreases, the exposure of the hydrophilic regions of the protein increases and proteins elute from the column in order of increasing hydrophobicity." *Id.* at col. 1 ll. 45–49.

During the loading step, only a finite amount of protein can bind to the matrix. If too much protein is loaded on the column, "'breakthrough' or loss of protein to the solution phase before elution" will occur. *Id.* at col. 3 ll. 40–41. The '707 patent claims a process that reduces breakthrough, or in other words, increases the "dynamic capacity" of a HIC column. Dynamic capacity refers to "the maximum amount of protein in solution which can be loaded onto a column without significant breakthrough or leakage of the protein into the solution phase of a column before elution." *Id.* at col. 3 l. 65–col. 4 l. 3.

Prior art methods of increasing a HIC column's dynamic capacity included using a higher salt concentration in the buffer solution. *See id.* at col. 3 ll. 37–38. This resulted in other problems, however, as "high salt can be detrimental to protein stability. High salt increases the viscosity of a solution, results in increased formation of aggregates, results in protein loss due to dilution and filtration of the protein after elution from the column, and can lead to reduced purity." *Id.* at col. 3 ll. 41–45. Instead of increasing the concentration of a single salt, the '707 invention:

> provides combinations of salts useful for increasing the dynamic capacity of an HIC column compared with the dynamic capacity of the column using separate salts alone. These combinations of salts allow for a decreased concentration of at least one of the salts to achieve a greater dynamic capacity, without compromising the quality of the protein separation.

Id. at col. 2 ll. 9–15. All of the '707 claims require a salt combination chosen from one of three pairs: citrate and sulfate, citrate and acetate, or sulfate and acetate. Representative claim 1 recites:

> 1. A process for purifying a protein on a hydrophobic interaction chromatography column such that the dynamic capacity of the column is increased for the protein comprising
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> mixing a preparation containing the protein with a combination of a first salt and a second salt,
>
> loading the mixture onto a hydrophobic interaction chromatography column, and eluting the protein,
>
> wherein the first and second salts are selected from the group consisting of citrate and sulfate, citrate and acetate, and sulfate and acetate, respectively, and
>
> wherein the concentration of each of the first salt and the second salt in the mixture is between about 0.1 M and about 1.0.

Id. at col. 15 ll. 8–18.

II

During prosecution, the examiner rejected the then-pending '707 claims as obvious in view of U.S. Patent No. 5,231,178 ("Holtz"). J.A. 174–75. The examiner noted that Holtz disclosed several salts for improving hydrophobic interactions between a protein and the column matrix. J.A. 174. According to the examiner, it would have been obvious for a person of ordinary skill to routinely optimize Holtz to achieve the claimed invention. J.A. 175.

On January 26, 2011, Amgen responded to the examiner's rejection, pointing out that "the pending claims recite a particular *combination* of salts. No combinations of salts

[are] taught nor suggested in the Holtz et al. patent, nor [are] the *particular* combinations of salts recited in the pending claims taught nor suggested in this reference." J.A. 182. Amgen further noted that the claimed invention is directed to increasing dynamic capacity of a HIC column and Holtz does not teach dynamic capacity at all. *See id*. It also attached a declaration from '707 patent inventor Anna Senczuk ("Declaration") for support. The Declaration states that the inventors discovered that using a sulfate/citrate or sulfate/acetate salt combination resulted in substantial increases in the dynamic capacity of a HIC column as compared to using a single salt. *See* J.A. 187 ¶ 3. It further explains that using a sulfate/citrate, sulfate/acetate, or acetate/citrate combination reduced purification costs on a commercial scale as compared to using only a single salt. *See* J.A. 187–88 ¶ 4. The Declaration did not discuss any salt pairs other than sulfate/citrate, sulfate/acetate, and acetate/citrate—the only claimed pairs in the '707 patent. Amgen's response highlighted the particular salt pairs disclosed in the Declaration:

> As pointed out in paragraph 4 of the Declaration, "The improvement resulting from the use of dual salts in HIC goes beyond merely optimizing a column to best suit a particular protein. Use of *this particular combination of salts* greatly improves the cost-effectiveness of commercial manufacturing by reducing the number of cycles required for each harvest and reducing the processing time for each harvest."

J.A. 183 (emphasis added) (quoting J.A. 188 ¶ 4).

On April 7, 2011, the examiner again rejected the claims. The examiner stated that "[a]pplicant contends that the instant claims recite a particular combination of salts. However, the examiner contends that the cited reference does disclose salts used in a method of purification" and that adjustment of conditions was within the skill of

an ordinary artisan. J.A. 949. On August 22, 2011, Amgen replied to the examiner's rejection and reiterated that Holtz does not disclose a combination of salts and does not disclose enhancing the dynamic capacity of a HIC column. *See* J.A. 160–61. Amgen pointed out that choosing a working salt combination was a "lengthy development path" and that "merely adding a second salt" would not result in the invention. J.A. 162. The examiner then allowed the claims.

III

In August 2016, Coherus filed an abbreviated Biologic License Application ("aBLA") seeking FDA approval to market a biosimilar version of Amgen's pegfilgrastim product Neulasta. Pegfilgrastim is a recombinant therapeutic protein that stimulates the production of neutrophils, a type of white blood cell. The parties exchanged information as required by the Biologics Price Competition and Innovation Act and determined that the '707 patent should be included in Amgen's infringement suit. Coherus's aBLA revealed that Coherus's manufacturing process contains several chromatography steps used to purify pegfilgrastim. One of the steps involves a chromatography buffer containing a salt combination, but not one of the specific combinations recited in the claims.

On May 10, 2017, Amgen sued Coherus for infringing the '707 patent based on Coherus's aBLA. Amgen alleged infringement under the doctrine of equivalents because the salt combination used in Coherus's process did not match any of the three expressly claimed salt combinations in the '707 patent. *See* J.A. 109–10 ¶ 50. Coherus then moved to dismiss Amgen's complaint under Federal Rule of Civil Procedure 12(b)(6).

The magistrate judge issued a Report and Recommendation ("Report"), recommending that Coherus's motion to dismiss be granted. *Amgen Inc. v. Coherus Biosciences Inc.*, No. 17-cv-546-LPS-CJB (D. Del. Dec. 7, 2017) (D.I. 50);

J.A. 12–30. The magistrate judge noted that, during prosecution, Amgen distinguished Holtz by arguing that Holtz did not disclose "one of the *particular*, recited combinations of salts."[1] J.A. 24. Based on this, the magistrate judge determined that Amgen "clearly and unmistakably—and indeed, repeatedly—indicated to competitors that it surrendered processes using combinations of salts different from the '*particular* combinations of salts recited in the . . . claims[.]'" J.A. 23. The Report concluded that "prosecution history estoppel bars Amgen from now attempting to reassert surrendered ground involving other combinations of salts." J.A. 28.

The district court adopted the magistrate judge's Report and granted Coherus's motion to dismiss. *See Amgen Inc. v. Coherus Biosciences Inc.*, No. 17-cv-546-LPS-CJB, 2018 WL 1517689, *1 (D. Del. Mar. 26, 2018) ("*Decision*"). It held that "[t]he prosecution history, namely, the patentee's correspondence in response to two office actions and a final rejection, shows a clear and unmistakable surrender of claim scope by the patentee." *Id.* at *2. The district court further held that, by disclosing but not claiming the salt combination used by Coherus, Amgen had dedicated that particular combination to the public. *Id.* at *3. It concluded that the dedication-disclosure doctrine formed an independent basis on which to dismiss Amgen's infringement claim. *See id.* Amgen appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

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[1] The magistrate judge also noted that, while directed to a different salt combination, Amgen made the same argument—that Holtz did not disclose the claimed "particular combination" of salts—during prosecution of the parent patent. J.A. 21–22.

DISCUSSION

I

We review an order dismissing a complaint for failure to state a claim under the law of the regional circuit, here the Third Circuit. *McZeal v. Sprint Nextel Corp.*, 501 F.3d 1354, 1355–56 (Fed. Cir. 2007). The Third Circuit reviews challenges to a dismissal for failure to state a claim de novo. *Sands v. McCormick*, 502 F.3d 263, 267 (3d Cir. 2007). "In evaluating the propriety of the dismissal, we accept all factual allegations as true, construe the complaint in the light most favorable to the plaintiff, and determine whether, under any reasonable reading of the complaint, the plaintiff may be entitled to relief." *Id.* at 267–68. "Whether prosecution history estoppel applies, and thus whether the doctrine of equivalents is available for a particular claim limitation, is a question of law reviewed de novo." *Spectrum Pharm., Inc. v. Sandoz Inc.*, 802 F.3d 1326, 1337 (Fed. Cir. 2015).

II

We agree with the district court that, during prosecution of the '707 patent, Amgen clearly and unmistakably surrendered salt combinations other than the particular combinations recited in the claims. Prosecution history estoppel thus bars Amgen from succeeding on its infringement claim under the doctrine of equivalents.

"Prosecution history estoppel applies as part of an infringement analysis to prevent a patentee from using the doctrine of equivalents to recapture subject matter surrendered from the literal scope of a claim during prosecution." *Trading Techs. Int'l, Inc. v. Open E Cry, LLC*, 728 F.3d 1309, 1322 (Fed. Cir. 2013). Prosecution history estoppel can occur in two ways: "either (1) by making a narrowing amendment to the claim ('amendment-based estoppel') or (2) by surrendering claim scope through argument to the patent examiner ('argument-based estoppel')." *Conoco, Inc.*

v. Energy & Envtl. Int'l, L.C., 460 F.3d 1349, 1363 (Fed. Cir. 2006). To invoke argument-based estoppel, "the prosecution history must evince a clear and unmistakable surrender of subject matter." *Id.* at 1364 (quoting *Deering Precision Instruments, LLC v. Vector Distribution Sys., Inc.*, 347 F.3d 1314, 1326 (Fed. Cir. 2003)).

"[W]here a patent applicant sets forth multiple bases to distinguish between its invention and the cited prior art, the separate arguments [can] create separate estoppels as long as the prior art was not distinguished based on the combination of these various grounds." *PODS, Inc. v. Porta Stor, Inc.*, 484 F.3d 1359, 1367 (Fed. Cir. 2007) (internal quotation marks omitted) (quoting *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1581–83 (Fed. Cir. 1995)). "[C]lear assertions made during prosecution in support of patentability, whether or not actually required to secure allowance of the claim, may also create an estoppel . . . [t]he relevant inquiry is whether a competitor would reasonably believe that the applicant had surrendered the relevant subject matter." *Id.* at 1368 (internal quotation marks omitted).

We hold that argument-based prosecution history estoppel applies here because Amgen clearly and unmistakably surrendered unclaimed salt combinations during prosecution. In its January 6, 2011 response, Amgen distinguished Holtz on the basis that Holtz did not teach or suggest the "*particular* combinations of salts" recited in Amgen's claims. J.A. 182. Indeed, Amgen emphasized "particular" and referred to its particular salts three times in the span of two pages. *See* J.A. 182–83. The Declaration attached to Amgen's response also highlights and discusses the same particular combinations recited in Amgen's claims. For example, the Declaration refers to sulfate/citrate and sulfate/acetate as "particular dual salt combination[s]" that resulted in increased dynamic capacity as compared to a single salt. J.A. 187. It also explains that using a sulfate/citrate, sulfate/acetate, or acetate/citrate

combination (the only claimed combinations) resulted in reduced commercial manufacturing costs as compared to using only a single salt. *See* J.A. 187–88. Notably, Amgen's response to the examiner's office action quotes the Declaration's conclusion that "[u]se of this particular combination of salts greatly improves the cost-effectiveness of commercial manufacturing by reducing the number of cycles required for each harvest and reducing the processing time for each harvest." J.A. 183 (quoting J.A. 188 ¶ 4). Amgen's response and Declaration do not mention any salt combinations other than those claimed.[2] Based on Amgen's statements during prosecution, we agree with the district court's conclusion that "a competitor would reasonably believe" that Amgen surrendered unclaimed salt combinations. *See PODS*, 484 F.3d at 1368.

Amgen argues that it did not distinguish Holtz on the basis that Holtz failed to disclose the particular claimed combinations, but rather, it distinguished Holtz on the basis that Holtz failed to disclose increasing dynamic capacity and failed to disclose any salt combinations at all. *See* Appellant Br. 30–36. According to Amgen, its statement regarding the "particular combinations" of salts "simply observes (correctly) as a factual matter that Holtz does not disclose using combinations of salts in the first instance," and thus does not clearly and unmistakably surrender unclaimed salt pairs. *Id.* at 35. We disagree.

In its January 6, 2011 response, Amgen asserted three bases for distinguishing Holtz: (1) "[n]o combinations of salts [are] taught nor suggested in the Holtz et al. patent"; (2) "nor [are] the *particular* combinations of salts recited in

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[2] That Amgen made the same "particular combination" argument with respect to the same prior art reference as to salts claimed in the parent patent further reflects Amgen's emphasis on the *particular* claimed combinations. *See* J.A. 1240.

the pending claims taught nor suggested in [Holtz],"; and (3) "[t]here is no description or suggestion in Holtz et al. for the use of any combination of salts to increase the dynamic capacity of a HIC." J.A. 182. So while Amgen did assert multiple reasons for why Holtz is distinguishable, our precedent instructs that estoppel can attach to each argument. "[W]here a patent applicant sets forth multiple bases to distinguish between its invention and the cited prior art, the separate arguments [can] create separate estoppels as long as the prior art was not distinguished based on the combination of these various grounds." *PODS*, 484 F.3d at 1367 (internal quotation marks omitted) (quoting *Southwall Techs.*, 54 F.3d at 1581–83). Amgen did not rely on the combination of its asserted grounds to distinguish Holtz, so prosecution history estoppel applies to the "particular combinations" ground regardless of the other two arguments Amgen made.

Amgen also argues that prosecution history estoppel does not apply because its August 22, 2011 response—the response after which the claims were ultimately allowed—did not contain the argument that Holtz failed to disclose the particular claimed salt combinations. *See* Appellant Br. 38–40. According to Amgen, the arguments made in its last response prior to allowance "must be the focus of any argument-based estoppel analysis." *Id.* at 40. Our case law does not support this argument. We recognize that Amgen did not include the "particular combinations" ground in its August 22, 2011 response to the patent office. *See* J.A. 160–62. This does not mean, however, that Amgen's prior statements are erased. There is no requirement that argument-based estoppel apply only to arguments made in the most recent submission before allowance. "[C]lear assertions made during prosecution in support of patentability, whether or not actually required to secure allowance of the claim, may also create an estoppel[.]" *PODS*, 484 F.3d at 1368 (quoting *Southwall Techs.*, 54 F.3d at 1583). We see nothing in Amgen's final

submission that disavows the clear and unmistakable surrender of unclaimed salt combinations made in Amgen's January 6, 2011 response.

Because we hold that prosecution history estoppel applies, we do not reach the issue of whether Amgen dedicated unclaimed salt combinations to the public.

CONCLUSION

We have considered Amgen's remaining arguments and find them unpersuasive. The district court did not err in determining that prosecution history estoppel bars Amgen from succeeding on its infringement claim under the doctrine of equivalents. Accordingly, we affirm the district court's order dismissing Amgen's complaint for failure to state a claim.

AFFIRMED