United States Court of Appeals for the Federal Circuit

THE MEDICINES COMPANY,
Plaintiff-Cross-Appellant

v.

MYLAN, INC., MYLAN PHARMACEUTICALS INC., BIONICHE PHARMA USA, LLC,
Defendants-Appellants

2015-1113, 2015-1151, 2015-1181

Appeals from the United States District Court for the Northern District of Illinois in No. 1:11-cv-01285, Judge Amy J. St. Eve.

Decided: April 6, 2017

PORTER F. FLEMING, Haug Partners LLP, New York, NY, argued for plaintiff-cross-appellant. Also represented by EDGAR HAUG, ANGUS CHEN.

SHANNON BLOODWORTH, Perkins Coie, LLP, Washington, DC, argued for defendants-appellants. Also represented by DAN L. BAGATELL, Hanover, NH; DAVID LEE ANSTAETT, AUTUMN N. NERO, DAVID R. PEKAREK KROHN, Madison, WI.

Before DYK, WALLACH, and HUGHES, *Circuit Judges*.

DYK, *Circuit Judge*.

The Medicines Company ("Medicines") is the owner of U.S. Patent Nos. 7,582,727 ("the '727 patent") and 7,598,343 ("the '343 patent"). In response to an Abbreviated New Drug Application ("ANDA") submitted by Mylan, Inc. ("Mylan"), Medicines filed suit in the United States District Court for the Northern District of Illinois alleging that Mylan's ANDA infringed claims 1–3, 7–10, and 17 of the '727 patent, and claims 1–3 and 7–11 of the '343 patent. Mylan counterclaimed seeking a declaration that the asserted claims were invalid.

The district court held on summary judgment that the asserted claims of the '343 patent were not infringed because Mylan did not satisfy the "efficient mixing" limitation of those claims. After conducting a bench trial, the court held that the asserted claims of the '727 patent *were* infringed because those claims did *not* include an "efficient mixing" limitation.

We hold that both the '727 and '343 patents include a "batches" limitation that requires batch consistency, which, according to the patents in suit, is achieved through efficient mixing. Efficient mixing is therefore required by the asserted claims of both patents. We further construe efficient mixing as defined by Example 5 of the patents' specification. We therefore reverse the district court's judgment of infringement with respect to the '727 patent, and affirm its summary judgment of noninfringement with respect to the '343 patent. We do not address the validity of the patents in suit.

BACKGROUND

I

The '727 and '343 patents are directed to pharmaceutical formulations—or "batches"—of the drug bivalirudin

produced through a process that consistently minimizes impurities. Bivalirudin is a synthetic peptide used to prevent blood clotting in patients undergoing cardiac catheterization. This clinical application arises from the drug's ability to act as a reversible inhibitor of thrombin, a key enzyme in the cascade of biochemical reactions responsible for the formation of blood clots. Bivalirudin's pharmacological properties were known in the art, well before the filing of the patents in suit, and were covered by a patent owned by Medicines that expired in 2015, U.S. Patent No. 5,196,404.

The claimed inventions of the '727 and '343 patents are directed to minimizing impurities in batches of bivalirudin that have been compounded with a base. *See* '727 patent, col. 2 ll. 19–22; '343 patent, col. 2 ll. 19–22. Bivalirudin as an active ingredient is typically distributed or sold as a dry powder that must be compounded with a base, before being reconstituted in a clinical setting and administered to a patient as an intravenous injection. Reconstitution involves dissolving the drug (in dry powder form) in an aqueous solvent such as water or saline. Because dissolving bivalirudin by itself (without a base) results in an acidic solution not suitable for injection, commercial forms of bivalirudin compound bivalirudin with a base, which increases the pH of the reconstituted drug to a clinically acceptable level.

II

Medicines received approval from the Food & Drug Administration ("FDA") to market a base-compounded bivalirudin drug product in 2000, and has sold the approved product since 2001 under the tradename ANGIOMAX®, well before the critical date of the patents in suit. In approving ANGIOMAX®, the FDA required Medicines to limit the level of "Asp^9-bivalirudin"—an impurity generated during the compounding process that shortens bivalirudin's shelf life—to less than 1.5 percent.

Asp^9-bivalirudin is formed when the ninth amino acid of bivalirudin's peptide chain converts from asparagine to aspartic acid. Consequently, Medicines was required to reject any ANGIOMAX® batch determined to have an Asp^9 level higher than 1.5 percent. *See United States v. Barr Labs., Inc.*, 812 F. Supp. 458, 471–72 (D.N.J. 1993); 21 C.F.R. § 211.165(f).

Between 2001 and 2005, Medicines and its contract manufacturer, Ben Venue Laboratories ("BVL"), produced and sold numerous batches of compounded bivalirudin having Asp^9 levels of less than 1.5 percent. Although the "old compounding process," *Medicines Co. v. Mylan Inc.*, 72 F. Supp. 3d 837, 850 (N.D. Ill. 2014), used by Medicines and BVL to produce ANGIOMAX® "resulted in variable and sometimes high levels of Asp^9 impurities," *id.* at 847, the overriding majority of these batches in fact had Asp^9 levels below 0.6 percent (the level specified in the asserted claims). As the district court observed, "79 of 87 prior art ANGIOMAX® batches had Asp^9 levels at or below about 0.6% and [Medicines] sold dozens of these batches prior to the critical date." *Id.* at 864.

In 2005 and 2006, however, Medicines produced two batches of ANGIOMAX® with Asp^9 levels above the 1.5 percent limit specified by the FDA. After failing to solve the problem of inconsistent batches internally, Medicines retained a consultant, Dr. Gary Musso, who together with Dr. Gopal Krishna, an employee of Medicines at the time, identified the compounding process used by BVL as the source of the problem. Drs. Krishna and Musso are the named co-inventors of the '727 and '343 patents.

The process of compounding bivalirudin generally involves three steps: (1) forming a bivalirudin solution by dissolving the drug in an aqueous solution; (2) mixing the bivalirudin solution with a pH-adjusting solution containing a base; and (3) removing solvents to yield the final compounded drug product. *See Medicines*, 72 F. Supp. 3d

at 843. The '727 and '343 patents explain that in mixing the pH-adjusting solution into the bivalirudin solution, "concentrated sites in the compounding solution that have much higher pH levels" are formed. *See, e.g.*, '727 patent, col. 9 ll. 20–22. These localized "hot spots" catalyzed the degradation of bivalirudin to Asp^9-bivalirudin, resulting in undesirable high levels of the impurity in some instances. *See, e.g.*, *id.* col. 9 l. 19.

Based on this principle, Drs. Krishna and Musso developed an improved, "efficient mixing" process for mixing the pH-adjusting solution with the bivalirudin solution that minimized the formation of these hotspots. *See Medicines*, 72 F. Supp. 3d at 848. This improved "efficient mixing" process resulted in batches that consistently satisfied the FDA's 1.5 percent limit on the level of Asp^9-bivalirudin. Moreover, based on Drs. Krishna and Musso's experiments, Medicines discovered that the Asp^9 level of batches compounded using the improved "efficient mixing" process never exceeded 0.6 percent. *See id.* at 848–49.

This batch consistency of bivalirudin drug products compounded using "efficient mixing" is the invention disclosed and claimed by the patents in suit, which were filed on the same day and share nearly identical specifications. *See Medicines Co. v. Mylan Inc.*, 2012 WL 3234282, at *2 (N.D. Ill. Aug. 6, 2012).

Representative claim 1 of the '727 patent provides:

> 1. Pharmaceutical batches of a drug product comprising bivalirudin . . . wherein the batches have a pH adjusted by a base, said pH is about 5-6 when reconstituted in an aqueous solution for injection, and *wherein the batches have a maximum impurity level of Asp^9-bivalirudin that does not exceed about 0.6%* as measured by HPLC.

'727 patent, col. 25 ll. 56–64 (emphasis added).

> Representative claim 1 of the '343 patent provides:
>
> 1. Pharmaceutical batches of a drug product comprising bivalirudin . . . prepared by a compounding process comprising:
>
> > (i) dissolving bivalirudin in a solvent to form a first solution;
> >
> > (ii) efficiently mixing a pH-adjusting solution with the first solution to form a second solution, wherein the pH-adjusting solution comprises a pH-adjusting solution solvent; and
> >
> > (iii) removing the solvent and pH-adjusting solution solvent from the second solution;
>
> wherein the batches have a pH adjusted by a base, said pH is about 5-6 when reconstituted in an aqueous solution for injection, and *wherein the batches have a maximum impurity level of Asp^{9}-bivalirudin that does not exceed about 0.6%* as measured by HPLC.

'343 patent, col. 27 ll. 13–31 (emphasis added).

The emphasized claim limitation is common to both patents, and we refer to this shared limitation as the "batches limitation." The term "pharmaceutical batches" is defined by the patents as follows:

> As used here, "batch" or "pharmaceutical batch" refers to material produced by a single execution of a compounding process of various embodiments of the present invention. "Batches" or "pharmaceutical batches" as defined herein may include a single batch, wherein the single batch is representative of all commercial batches (see generally, Manual of Policies and Procedures, Center for Drug Evaluation and Research, MAPP 5225.1,

> Guidance on the Packaging of Test Batches at 1), and wherein the levels of, for example, Asp^9-bivalirudin, total impurities, and largest unknown impurity, and the reconstitution time represent levels for all potential batches made by said process. "Batches" may also include all batches prepared by a same compounding process."

'727 patent, col. 5 ll. 24–36; '343 patent, col. 5 ll. 24–36.

III

Seeking to market a generic version of ANGIOMAX®, Mylan submitted an ANDA to the FDA in 2010. In its ANDA, Mylan stated that it would limit the Asp^9 level of its generic product to less than 2.0 percent. *See Medicines*, 72 F. Supp. 3d at 846. Mylan also made a paragraph IV certification under the provisions of the Hatch-Waxman Act, 21 U.S.C. § 355(j)(2)(A)(vii)(IV), asserting that its product would not infringe the '727 and '343 patents (listed in the FDA's Orange Book), or that these patents were invalid. In response, Medicines filed suit in the district court alleging infringement of the '727 and '343 patents under 35 U.S.C. § 271(e)(2). Mylan filed counterclaims seeking declaratory judgments of invalidity.

The parties disputed the meaning of two claim terms: "pharmaceutical batches" and "efficiently mixing." With respect to "pharmaceutical batches," the district court construed the term consistent with the definition set forth in the patents' specification to refer to either: (1) "a single batch, wherein the single batch is representative of all commercial batches . . . *made by a compounding process*, and wherein the levels of, for example, Asp^9-bivalirudin, total impurities, and largest unknown impurity, and the reconstitution time represent levels for all potential batches made by said process"; or (2) "all batches prepared by a same compounding process." *Medicines*, 2012 WL 3234282, at *3–5 (emphasis added). The district court's construction—to which both parties ultimately

consented—adds the emphasized language to the specification's definition of "batches," thereby clarifying that the definition requires a particular process. *See id.* at *5.

With respect to "efficiently mixing," the district court relied on two examples set forth in the patents' specifications comparing Medicines' "old compounding process" using "inefficient mixing conditions" (Example 4) with the improved "efficient mixing" process developed by Drs. Krishna and Musso (Example 5). *See id.* at *14–15; *see also* '727 patent, col. 21 l. 44–col. 24 l. 35; '343 patent, col. 22 l. 21–col. 25 l. 3. The court ultimately agreed that Medicines had disclaimed the "inefficient mixing conditions" of Example 4 and adopted Mylan's proposed construction of "efficiently mixing" to require "not using inefficient mixing conditions such as described in Example 4." *Medicines*, 2012 WL 3234282, at *15.

Based on these claim constructions, the district court held on summary judgment that Mylan's ANDA did not infringe the '343 patent because the material facts concerning Mylan's compounding process were not in dispute and these "undisputed facts show[ed] that Mylan's compounding process is more inefficient than the 'inefficient mixing' process" of Example 4. *See Medicines Co. v Mylan Inc.*, 2013 WL 6633085, at *10 (N.D. Ill. Dec. 16, 2013). With respect to the '727 patent, however, the court held that "efficiently mixing" was not a claim limitation and determined that factual disputes concerning the Asp^9 level of Mylan's ANDA product precluded summary judgment. *See id.* at *20.

The district court conducted a six-day bench trial with respect to infringement and validity of the '727 patent. In its post-trial opinion, the court rejected Mylan's invalidity contentions and held that Mylan's ANDA infringed the '727 patent as a matter of law. In so holding, the district court appeared to assume that any batch with an Asp^9 level below 0.6 percent would infringe the claims, even

though the court had earlier determined that the prior art disclosed such batches. The court reasoned that "Mylan's ANDA specification [would] allow[] it to market a drug product with Asp[9] . . . levels from 0.0%–2.0%, a range that includes the '727 patent's claimed ranges of 0.0–0.6%," and "[w]hat a generic applicant asks for and receives approval to market, if within the scope of a valid claim, is an infringement." *See Medicines*, 72 F. Supp. 3d at 883–85 (quoting *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1279 (Fed. Cir. 2013)). The court again rejected Mylan's argument that the claims of the '727 patent required "efficient mixing" and entered final judgment in favor of Medicines on all claims and counterclaims with respect to the '727 patent. *Id.* at 886–88.

Mylan has appealed the district court's judgment of infringement and no invalidity of the '727 patent, and Medicines has cross-appealed the district court's summary judgment of noninfringement of the '343 patent. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

IV

Shortly after the completion of briefing in this case, the panel issued an opinion holding the '727 and '343 patents invalid under the on-sale bar of 35 U.S.C. § 102(b) based on pre-critical date batches of ANGIOMAX® produced by BVL for Medicines. *See Medicines Co. v. Hospira, Inc.*, 791 F.3d 1368, 1372 (Fed. Cir. 2015). Accordingly, in this case, we reversed the district court's judgment with respect to the '727 patent and dismissed Medicines' cross-appeal regarding the '343 patent as moot.

The full court subsequently granted Medicines' petition for rehearing en banc in *Hospira*, and on rehearing held that Medicines' relationship with BVL did not give rise to an invalidating "commercial offer for sale" under *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 57–68 (1998). *See Medicines Co. v. Hospira, Inc.*, 827 F.3d 1363, 1373–74 (Fed. Cir. 2016) (en banc). We reopened and stayed

this appeal when the court granted rehearing in *Hospira*. Following the court's en banc decision, we requested the parties submit supplemental briefs. We now decide this appeal on the merits.[1]

DISCUSSION

Our review of the district court's summary judgment is plenary. *See, e.g.*, *Glaxo Grp. Ltd. v. TorPharm, Inc.*, 153 F.3d 1366, 1370 (Fed. Cir. 1998). We review the district court's factual findings after a bench trial for clear error and the court's legal conclusions *de novo*. *See, e.g.*, *Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d 1349, 1358 (Fed. Cir. 2014). The district court's claim constructions present pure questions of law subject to *de novo* review because the court made no factual findings concerning extrinsic evidence in construing the disputed claim terms. *See, e.g.*, *In re Papst Licensing Dig. Camera Patent Litig.*, 778 F.3d 1255, 1261 (Fed. Cir. 2015).

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[1] Although Mylan's appeal calls into question the validity of the patents in suit, Mylan's counsel agreed that a finding of noninfringement would render it unnecessary for the court to reach this issue. *See* Oral Argument at 1:14, *Medicines Co. v. Mylan, Inc.*, No. 15-1113 (Fed. Cir. Dec. 6, 2016). Under *Cardinal Chemical Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 99 (1993), a finding of noninfringement cannot moot a counterclaim of invalidity, but we retain the discretion to limit the grounds upon which appeals are decided. Here, because Mylan has agreed that a judgment of noninfringement with respect to both patents in suit "would be tantamount to the relief sought on the merits" and that we need not reach the invalidity issues, we decline to reach the merits of Mylan's invalidity contentions. *See Old Town Canoe Co. v. Confluence Holdings Corp.*, 448 F.3d 1309, 1318 n.2 (Fed. Cir. 2006).

I

Mylan argues on appeal that the district court erred by declining to interpret the claims of the '727 patent to require "efficient mixing" as part of the batches limitation. We agree with Mylan that "efficient mixing" is required by the batches limitation and is therefore a limitation of both the '727 and '343 patents.

The batches limitation restricts the claims of the '727 patent (as well as the '343 patent) to "batches hav[ing] a maximum impurity level of Asp^9-bivalirudin that does not exceed about 0.6%." At the outset, we note that the batches limitation cannot be literally construed to cover individual batches of base-compounded bivalirudin having Asp^9 levels that "do[] not exceed about 0.6%." Such a construction would render the claims of the '727 patent invalid in light of Medicines' numerous pre-critical-date sales of ANGIOMAX® batches having Asp^9 levels below 0.6 percent. *See Medicines*, 72 F. Supp. 3d at 864.

Rather, properly construed, what the batches limitation requires is the use of a process that achieves batch consistency. This requirement follows from simply reading the batches limitation against the specification's definition of the term "batches," as slightly revised by the district court with the agreement of the parties to clarify that the "batches" must be made by a particular compounding process. *See Medicines*, 2012 WL 3234282, at *5. That definition limits the "batches" claimed by the patents in suit to either "all batches prepared by *a same compounding process*," or "a single batch . . . wherein the levels of [Asp^9-bivalirudin] represent levels for all potential batches *made by said process*." '727 patent, col. 5 ll. 24–36 (emphasis added); '343 patent, col. 5 ll. 24–36. The batches limitation therefore requires a process that achieves consistency between batches produced from the "same compounding process"—*i.e.*, batch consistency.

There is no real dispute that the claims require batch consistency vis-à-vis the batches limitation. Indeed, to the extent that Medicines' "old compounding process" resulted in ANGIOMAX® batches having inconsistent Asp[9] levels, *see Medicines*, 72 F. Supp. 3d at 850, Medicines agrees that batch consistency is the "result of following the patent[s in suit]" and is what "distin[guishes] [them] from the prior art." *See* Oral Argument at 1:44, *Medicines Co. v. Hospira, Inc.*, No. 14-1469 (Fed. Cir. Dec. 6, 2016); *id.* at 3:17 ("Q. The point six limitation is not enough to distinguish the prior art . . . it's the consistency limitation, right? A. Yes.").

The patentee, however, takes the position that the batches limitation is not necessarily limited to a compounding process that achieves batch consistency. Instead, according to Medicines, the batches limitation is satisfied whenever an accused infringer consistently produces batches having Asp[9] levels below 0.6 percent, and that the claims do not require the use of a particular process that achieves batch consistency.

We disagree, for several reasons. First, adopting Medicines' interpretation of the batches limitation would yield an unworkable claim construction. Under Medicines' interpretation, proof of infringement would necessitate forward-looking assessments of whether an accused infringer's production of future or "potential" batches would be likely to generate Asp[9] levels greater than "about 0.6%." To illustrate, if a defendant using the same compounding process produced fifty batches each having an Asp[9] level below 0.6 percent, each of those fifty batches would infringe. But the defendant would not know whether any of the batches infringed until all fifty batches had been produced because if even one of those batches was determined to have an Asp[9] level higher than 0.6 percent, none of the batches would infringe. *See* Oral Argument at 17:00–19:06, *Medicines Co. v. Mylan, Inc.*, No. 15-1113 (Fed. Cir. Dec. 6, 2016). For an ongoing commercial com-

pounding process, this approach cannot provide "reasonable certainty" regarding the scope of the asserted claims. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2129 (2014); *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1384 (Fed. Cir. 2003) ("A claim is indefinite if its legal scope is not clear enough that a person of ordinary skill in the art could determine whether a particular composition infringes or not."); *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470 (Fed. Cir. 1993) ("[C]laims. . . [must be] sufficiently precise to permit a potential competitor to determine whether or not he is infringing.").

Medicines' interpretation also fails to consider the specification and prosecution history of the patents in suit, both of which demonstrate that the invention disclosed by the '727 and '343 patents is a compounding process that achieves batch consistency. The specification, for example, states that "development of a *compounding process for formulating bivalirudin* that *consistently* generates formulations having low levels of impurities is desirable," '727 patent, col. 2 ll. 19–21 (emphasis added), and that "*the compounding process . . . of the invention described herein* may consistently generate pharmaceutical batches . . . having the same characteristics, *id.* col. 13 ll. 10–13 (emphasis added).

During prosecution of the '727 patent (as well as the '343 patent), Medicines further represented that "[i]n the present invention, various embodiments relate to a less subjective and more consistent *process* for the mixing of the pH-adjusting solution with the bivalirudin solution." J.A. 20122 (emphasis added). Medicines also took pains to distinguish its pre-critical date sales of ANGIOMAX® in observing that "[p]harmaceutical batches . . . as described [by the patents in suit], *and as prepared by the new process of the present invention* . . . have not been on sale/marketed/or offered for sale for more than one (1) year as of the [patents'] filing date." *Id.* (emphasis added).

Finally, any remaining doubt that the batches limitation requires a compounding process is dispelled by Medicines' admission to the district court that "[w]hen viewed in the context of the specification, it is readily apparent that the [definition of 'pharmaceutical batches'] refers to the compounding processes described in the patents-in-suit." *Medicines*, 2013 WL 6633085, at *15.

Thus, we reject Medicines' interpretation and conclude that the batches limitation requires the use of a compounding process that achieves batch consistency. In doing so, we note that our decision does not impermissibly add a process limitation to a product claim that does not require a process because the specification's definition of "batches" by itself injects a compounding process as a limitation in the asserted claims.[2]

The question remains as to what that compounding process entails. Based on the intrinsic evidence of the patents in suit, the answer is that the compounding process must use efficient mixing.

The patents' specification unequivocally states that the "pH-adjusting solution *will be efficiently mixed*," and that "[e]fficient mixing of the pH-adjusting solution . . . *will* minimize levels of Asp[9]-bivalirudin." *See* '727 patent, col. 8 ll. 54–58 (emphasis added); '343 patent, col. 8 ll. 54–58. Indeed, apart from efficient mixing, no part of the patents' disclosure teaches another method capable of producing consistent batches. In comparing the batches resulting from the "inefficient mixing conditions" of Example 4 with those from the "efficient mixing conditions" of Example 5, the specification teaches that "the charac-

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[2] *See, e.g.*, *Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1344 (Fed. Cir. 2008); *Vanguard Prods. Corp. v. Parker Hannifin Corp.*, 234 F.3d 1370, 1372 (Fed. Cir. 2001).

teristics of the batches generated by [Example 4] may be variable," and that "the [efficient mixing] process demonstrated in Example 5 produced batches *generally and consistently* having lower levels of impurities than the [inefficient mixing] process of Example 4." '727 patent, col. 22, ll. 25–28, col. 23 ll. 24–26 (emphasis added); '343 patent, col. 23 ll. 1–4, col. 23 ll. 62–65. Finally, the specification teaches that consistent "batch(es) may be prepared by a compounding process comprising dissolving bivalirudin in a solvent to form a bivalirudin solution, *efficiently mixing* a pH-adjusting solution with the bivalirudin solution to form a compounding solution, and removing solvents from the compounding solution. This compounding process *includes all* of the embodiments as described." '727 patent, col. 15 ll. 14–20 (emphasis added); '343 patent, col. 15 ll. 14–20. The specification therefore teaches efficient mixing as a necessary and sufficient condition for achieving batch consistency.

The prosecution history confirms that achieving batch consistency requires efficient mixing. Medicines expedited the examination of the applications giving rise to the '727 and '343 patents by filing substantially the same Petition to Make Special in both applications.[3] *See Medicines*, 2013

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[3] Under regulations in force at the time, an applicant seeking accelerated examination in the U.S. Patent & Trademark Office ("PTO") through a Petition to Make Special was required to conduct a "pre-examination search" of the prior art and to file an Information Disclosure Statement citing "references deemed most closely related to the subject matter encompassed by the claims." *See* Manual of Patent Examining Procedure ("MPEP") ch. 708.02(a) (8th ed. Sept. 2007); *see also* 71 Fed. Reg. 36,323, 36,325 (June 26, 2006). The regulations further required the filing of an "accelerated examination support document" requiring petitioners to provide "a detailed

WL 6633085, at *5. In these petitions, Medicines explained the problem of high Asp^9 levels of batches from its "old compounding process" and stated that "various embodiments" of the "present invention . . . relate to a less subjective and more consistent process for the mixing of the pH-adjusting solution with the bivalirudin solution. This process involves *efficiently mixing* the pH-adjusting solution and the dissolved bivalirudin solution, which is not performed in the Applicants' prior compounding process." J.A. 20122 (emphasis added).

After considering the same intrinsic evidence we have just summarized, the district court concluded that Medicines had disclaimed inefficient mixing. *See Medicines*, 2012 WL 3234282, at *12–14; *see also Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995). Whether we view the patentee as having disclaimed inefficient mixing or construe "batches" to require efficient mixing, *see Trustees of Columbia Univ. v. Symantec Corp.*, 811 F.3d 1359, 1363–64 (Fed. Cir. 2016), at bottom, the compounding process must be one that uses efficient mixing.

Medicines urges that reading the batches limitation to require "efficient mixing" would render the asserted claims of the '343 patent—which already recite an "efficiently mixing" step—superfluous, and that the batches limitation extends to compounding processes that do not use efficient mixing. This is not correct. The recitation of other product-by-process limitations in the claims of the '343 patent—"dissolving bivalirudin in a solvent to form a first solution" and "removing the solvent and pH-adjusting solution solvent"—means that the claims of the patents in suit would merely overlap, and "overlapping

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explanation of how each of the claims are patentable over the references cited." These requirements appear to be applicable to current patent applications as well. *See* MPEP 708.02(a) (9th ed. Nov. 2015).

patent claims are not unusual." *Andersen Corp. v. Fiber Composites, LLC*, 474 F.3d 1361, 1370 (Fed. Cir. 2007). Divorcing efficient mixing from the batches limitation would also have the impermissible result of "extend[ing] [Medicines'] monopoly beyond the invention" disclosed, and potentially to the prior art.[4] *Gen. Elec. Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 371 (1938); *Plummer v. Sargent*, 120 U.S. 442, 449 (1887); *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293, 309–11 (1884).

For all these reasons, the reading of the batches limitation that "most naturally aligns with the patent's description of the invention" is one that requires "efficient mixing." *Phillips*, 415 F.3d at 1316. And "[a]lthough [the '727 patent's] claim language does not expressly recite [efficient mixing], that is what they mean . . . The situation here involves specifications that in all respects tell us what the claims mean, buttressed by statements made during prosecution . . . Accordingly, to attribute to the claims a meaning broader than any indicated in the patents and their prosecution history would be to ignore the totality of the facts of the case and exalt slogans over real meaning." *Ormco Corp. v. Align Tech., Inc.*, 498 F.3d 1307, 1316 (Fed. Cir. 2007).

II

The next question is what is meant by "efficient mixing." Medicines argues that the patents' common specification defines "efficient mixing" as "mixing [that] is characterized by minimizing levels of Asp^9-bivalirudin in the compounding solution," *i.e.*, below 0.6 percent Asp^{9-}

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[4] As practiced by Medicines in the prior art, batch consistency was achieved pursuant to FDA regulations by rejecting batches having higher-than-acceptable Asp^9 levels. *See* 21 C.F.R. § 211.165(f).

bivalirudin in the intermediate solution.[5] Medicines argues that this definition is controlling. We disagree. Although this statement is taken verbatim from the specification, *e.g.*, '727 patent, col. 9 ll. 34–35, it does not purport to be definitional because it does not accord with the linguistic formula used by the patentee to signal the designation of other defined terms—including "batches." *See* '727 patent, col. 5 ll. 24–36; *see also, e.g.*, *id.* col. 5 ll. 37–38 (defining "drug product"); *id.* col. 5, ll. 46–53 (defining "carrier"). As the district court observed, in defining terms, "the patentees use[d] a similar format: the defined term in quotation marks, followed by the terms 'refers to' or 'as defined herein.'" *Medicines*, 2012 WL 3234282, at *9; *see also* '343 patent, col. 5 ll. 24–53. Because it departs from this format, the statement Medicines relies on lacks the clear expression of intent necessary for a patentee to act as its own lexicographer. *See, e.g.*, *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1370 (Fed. Cir. 2005).

More importantly, Medicines' construction is problematic because it amounts to a mere recitation of the results obtained from "efficient mixing" rather than a definition of what the efficient mixing process *is*. Before the district court, Medicines "conced[ed] that its proposed definition . . . construes that term functionally—*i.e.*, by its intended result." *Medicines*, 2012 WL 3234282, at *11.

Although functional limitations in patent claims are not *per se* objectionable even when the means-plus-

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[5] The patents' specification provides that the term "'[m]inimize' as used herein refers to the generation of a level of Asp^9-bivalirudin in the compounding solution that is less than about 0.6%." '727 patent, col. 8 ll. 58–60; '343 patent, col. 8 ll. 58–60.

function format is not invoked,[6] they cannot be "so broad that [they] cause[] the claim to have a potential scope of protection beyond that which is justified by the specification disclosure." *In re Swinehart*, 439 F.2d 210, 213 (C.C.P.A. 1971). Here, Medicines' construction would expand the scope of "efficient mixing" to cover any way of mixing that achieves a compounding solution having an Asp[9] level of less than 0.6 percent. The patentee's construction of "efficient mixing" thus attempts to claim all solutions to the identified "impurities" problem, without describing the entire range of solutions to that problem. Medicines' construction is therefore not permissible. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352–53 (Fed. Cir. 2010) (en banc) ("Such claims merely recite a description of the problem to be solved while claiming all solutions to it and . . . cover any [solution] later actually invented and determined to fall within the claim's functional boundaries—leaving it to [others] to complete an unfinished invention."); *see also Bayer CropScience AG v. Dow AgroSciences LLC*, 728 F.3d 1324, 1330–31 (Fed. Cir. 2013). Rather, efficient mixing must be defined in terms of the particular process or processes identified in the specification.

There is no contention that "efficient mixing" carries an accepted meaning to one of ordinary skill in the art. We therefore turn to the remainder of the specification, "the single best guide to the meaning of a disputed term" and "a concordance for the claims" to determine the process of efficient mixing. *Phillips*, 415 F.3d at 1315. The specification's detailed description teaches that "[e]fficient mixing . . . may be achieved through various methods. One such method may be to add . . . the pH-adjusting

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[6] There is no contention here that that claims are means-plus-function claims governed by 35 U.S.C. § 112(f) (formerly 35 U.S.C. § 112 ¶ 6).

solution and bivalirudin solution portion-wise." '727 patent, col. 9 ll. 34–38; '343 patent, col. 9, ll. 34–38. "Efficient mixing may also be achieved by adding the pH-adjusting solution to the bivalirudin solution at a constant rate . . . [or] at [a] variable rate . . . ." '727 patent, col. 10 ll. 17–32; '343 patent, col. 10 ll. 17–32. "Furthermore, efficient mixing may be achieved through the use of one or more mixing devices . . . [such as] a paddle mixer, magnetic stirrer, shaker, re-circulating pump, homogenizer, and any combination thereof. The mixing rate of . . . a paddle mixer may be between about 100 rpm and 1000 rpm . . . The mixing rate for . . . a homogenizer (*i.e.*, high shear mixing) may be between about 300 and about 6000 rpm . . . The mixing device may mix continuously . . . or at specific periods of time." '727 patent, col. 10 ll. 42–61; '343 patent, col. 10 ll. 42–61. "Moreover, efficient mixing may be achieved through adding the pH-adjusting solution to specific sites within the bivalirudin solution . . . In cases wherein a mixing device is used, the pH-adjusting solution may be added to the site of the mixing device . . . ." '727 patent, col. 11 ll. 10–16; '343 patent, col. 11 ll. 10–16.

In our view, these portions of the specification's detailed description of efficient mixing are "vague and unhelpful." *Finnigan Corp. v. ITC*, 180 F.3d 1354, 1364 (Fed. Cir. 1999). Rather than teaching what efficiently mixing *is*, the detailed description provides a laundry list of mixing techniques that individually (or in combination) may (or may not) constitute efficient mixing. Thus, unsurprisingly, neither the district court nor the parties relied on this portion of the specification to ascertain the meaning of "efficient mixing." *See Medicines*, 2012 WL 3234282, at *8–14. We similarly decline to do so.

Apart from the detailed description, two embodiments disclosed by the specification—Examples 4 and 5—clearly state what efficient mixing is and is not.

Example 4 describes "inefficient mixing":

> *Example 4: Effects of Rapidly Adding pH Adjusting Solution to the Bivalirudin Solution Under Inefficient Mixing Conditions—Large Scale Study*
>
> The pH-adjusting solution was added to the bivalirudin solution either all at once, or rapidly in multiple portions, while the bivalirudin solution was mixed by two paddle mixers located at the top and bottom of the bivalirudin solution. Both paddle mixers operated at a rate of between about 400 and about 800 rpm.

'727 patent, col. 21 ll. 44–64; '343 patent, col. 22 ll. 23–42.

Example 5 describes "efficient mixing":

> *Example 5: Effects of Adding pH Adjusting Solution at a Constant Rate and Under Efficient Mixing Conditions—Large Scale Study*
>
> The pH-adjusting solution was added to the bivalirudin solution at a controlled rate of 2 L/min using a peristaltic pump. A homogenizer was used to provide a high shear mixing environment (between about 1000 rpm and 1300 rpm) within the bivalirudin solution as the pH-adjusting solution was added[.] A feed tube extended from the peristaltic pump to an inlet in the homogenizer, so that the pH-adjusting solution was added to the bivalirudin solution at a site adjacent to the blades of the homogenizer. Simultaneously, a paddle mixer was used for mixing (mixing rate of between about 300 rpm and 700 rpm) near the surface of the bivalirudin solution.

'727 patent, col. 22 ll. 30–58; '343 patent, col. 23 ll. 6–31.

The district court relied on the "inefficient mixing conditions" of Example 4 to construe "efficient mixing" as "not using inefficient mixing conditions such as described

in Example 4." *Medicines*, 2012 WL 3234282, at *15. On appeal, Medicines repeatedly criticizes the court's negative construction as failing to define what "efficient mixing" is, as opposed to what it is not.[7] Although there is no *per se* rule against negative constructions, *see Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1329 (Fed. Cir. 2003), Medicines' argument carries some force. The logic of the argument suggests that that we should look to the specification's only clear delineation of what "efficient mixing" is—Example 5.

Critically, Medicines relied on the mixing parameters of Example 5 to overcome prior art cited during prosecution and did not cite any other examples of efficient mixing—including the generic teachings of the detailed description. In response to an anticipation rejection based on inherency, Medicines argued that the properties of the batches obtained from the mixing conditions of Example 5 were not "inherent . . . but rather [were] influenced by the process used to generate the product." J.A. 20182. Medicines emphasized that although Example 4 used "two paddle mixers located at the top and bottom of the bivalirudin solution" and "added . . . the bivalirudin solution either all at once, or rapidly in multiple portions," "the batches of Example 5 were prepared by a different proto-

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[7] *See Medicines*, 2012 WL 3234282, at *15; *see also, e.g.*, Medicines Revised Principal and Response Brief 30 ("This construction is flawed because it only defines ['efficient mixing'] in a negative manner, by what it is not—*without describing what 'efficient mixing' is*." (emphasis in original)); *id.* at 61 ("The district court's efficiently mixing construction is erroneous because it only defines the term in a negative manner, by what it is not, instead of what it is."); Medicines Revised Reply Brief 13 ("[A] proper construction of 'efficient mixing' should focus on what 'efficient mixing' is . . . .").

col" in which "the pH-adjusting solution was added to the bivalirudin solution at a controlled rate of 2L/min using a peristaltic pump," and that "[a] homogenizer was used to provide a high shear mixing environment (between about 1000 rpm and 1300 rpm) within the bivalirudin solution as the pH-adjusting solution was added." *Id.*

We conclude that one of ordinary skill in the art would rely on Example 5 to ascertain the metes and bounds of "efficiently mixing." As the only embodiment of efficient mixing, Example 5 is "highly indicative of the scope of the claims." *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1355 (Fed. Cir. 1998).[8] Example 5, however, is not merely the only disclosed *embodiment* of efficient mixing—it is the only *description* of efficient mixing in the patents in suit that casts light on what efficient mixing is and that enables one of ordinary skill in the art to achieve the objects of the claimed invention. Although the specification provides that Example 5 is "non-limiting," *e.g.*, '727 patent, col. 16 l. 6, no other part of the patents' written description sufficiently teaches the affirmative steps that constitute efficient mixing. In this circumstance, we think it entirely appropriate to limit the term "efficiently mixing" to the sole portion of the specification that adequately discloses "efficient mixing" to the public. *See Alloc, Inc. v. ITC*, 342 F.3d 1361, 1370 (Fed. Cir. 2003); *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1344–45 (Fed. Cir. 2001).

When held against the detailed description's open-ended and vague teachings regarding "efficient mixing,"

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[8] *See also, e.g.*, *Fenner Invs., Ltd. v. Cellco P'ship*, 778 F.3d 1320, 1323 (Fed. Cir. 2015) ("Any explanation, elaboration, or qualification presented by the inventor during patent examination is relevant, for the role of claim construction is to 'capture the scope of the actual invention' that is disclosed, described, and patented.").

Example 5 provides a clear "objective standard by which to measure the scope of the term." *Sonix Tech. Co. v. Publications Int'l, Ltd.*, 844 F.3d 1370, 1375 (Fed. Cir. 2017).[9] Accordingly, construing "efficiently mixing" to incorporate the efficient mixing conditions of Example 5 is necessary to "tether the claims to what the specification[] indicate[s] the inventor actually invented." *Retractable Techs., Inc. v. Becton, Dickinson & Co.*, 653 F.3d 1296, 1305 (Fed. Cir. 2011). In doing so, we adopt "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention . . . [which] in the end, [is] the correct construction." *Phillips*, 415 F.3d at 1312.

We therefore construe the "efficient mixing" required by the patents in suit to require using the efficient mixing conditions of Example 5.

III

The net effect of our claim construction is that to infringe either the '727 patent or the '343 patent, infringing batches must be compounded using a process that employs the efficient mixing conditions of Example 5. *See Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1291–95 (Fed. Cir. 2009) (en banc). Under this claim construction, Mylan's ANDA does not infringe the asserted claims since is undisputed that, for example, Mylan does not use multiple mixing devices as required by Example 5.

For completeness, we note the inapplicability under our claim construction of the district court's holding under *Sunovion*. The district court relied on the fact that Mylan's ANDA specifies an Asp^9 level of up to 2.0 percent,

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[9] *See also Columbia University*, 811 F.3d at 1366 ("The patentee cannot rely on its own use of inconsistent and confusing language in the specification to support a broad claim construction which is otherwise foreclosed").

a specification that, if approved, would "allow[] [Mylan] to produce all batches having less than 0.6% Asp[9] impurities." *Medicines*, 72 F. Supp. 3d at 886. The district court reasoned that, like the infringing ANDA in *Sunovion*, "Mylan's ANDA specification seeks approval for a bivalirudin drug product made from pharmaceutical batches allowed to have . . . [an] Asp[9] within the scope of the '727 patent's issued claims." *Id.* at 885–86. The court therefore held that "Mylan infringes as a matter of law." *Id.* at 886.

This holding rests on an incorrect claim construction of the '727 patent that does not require "efficient mixing."[10] *See id.* at 887. Under the correct claim construction, *Sunovion* is inapplicable because that decision "only applies when an ANDA specification defines a compound such that it meets the limitations of an asserted claim." *Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1382, 1387 (Fed. Cir. 2014) (internal quotation marks omitted). Mylan's ANDA does not on its face establish that Mylan's compounding process uses efficient mixing since, for example, nothing in the ANDA speaks to whether Mylan uses high-shear mixing as required by Example 5.

Instead, "[w]hen an ANDA is silent with respect to infringement . . . the correct analysis is . . . [whether] the ANDA applicant would likely sell an infringing composition pursuant to an approved ANDA." *Id.* at 1387–88 (internal quotation marks omitted) (quoting *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1570 (Fed. Cir. 1997)). In this case, the undisputed facts before the district court

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[10] While we also disagree with the district court's construction of "efficient mixing" as "not using inefficient mixing conditions such as described in Example 4," the district court correctly concluded that Mylan did not infringe the '343 patent under this construction because Mylan's compounding process was "more inefficient" than Example 4. *Medicines*, 2013 WL 6633085, at *9.

on summary judgment foreclose the possibility that Mylan "would likely sell an infringing" product. There is no genuine dispute that Mylan's compounding process "adds the pH-adjusting solution all at once" and "uses one paddle mixer" operating at 200 rpm. *Medicines*, 2013 WL 6633085, at *10 (internal quotation marks omitted). Example 5, however, requires multiple mixers and adds the pH-adjusting solution at a continuous rate using a peristaltic pump. *See* '727 patent, col. 22 ll. 46–64; '343 patent, col. 23 ll. 21–36. Accordingly, Mylan's ANDA cannot infringe the asserted claims of the '727 patent and the '343 patent.[11]

CONCLUSION

We reverse the district court's judgment of infringement with respect to the '727 patent and affirm the court's summary judgment of noninfringement with

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[11] Medicines argues that Mylan achieves efficient mixing by mixing a smaller solution volume than described in Example 5, using a pH-adjusting solution having a higher concentration of base, and using a higher mannitol concentration in the bivalirudin solution and no mannitol in the pH-adjusting solution. We disagree with Medicines that these differences create a genuine dispute of material fact regarding infringement. The detailed description of "efficient mixing" set forth in the patents' specification does not teach achieving efficient mixing by adjusting volume or concentration—to the contrary, the patent teaches "once the compounding solution is formed," adjusting the "final volume" is "[o]ptional," and that the "methods" for doing so are "known in the art." '727 patent, col. 11 ll. 25–30; '343 patent, col. 11, 25–30. Examples 4 and 5 use the same volumes and concentrations, which confirms that these parameters are irrelevant to "efficient mixing."

respect to the '343 patent. Accordingly, the judgment of the district court is

REVERSED IN PART AND AFFIRMED IN PART