United States Court of Appeals for the Federal Circuit

ASTRAZENECA AB, ASTRAZENECA PHARMACEUTICALS LP,
Plaintiffs-Appellees

v.

MYLAN PHARMACEUTICALS INC., KINDEVA DRUG DELIVERY L.P.,
Defendants-Appellants

2021-1729

Appeal from the United States District Court for the Northern District of West Virginia in No. 1:18-cv-00193-IMK-RWT, 1:19-cv-00203-IMK, Judge Irene M. Keeley.

Decided: December 8, 2021

DAVID I. BERL, Williams & Connolly LLP, Washington, DC, argued for plaintiffs-appellees. Also represented by ARTHUR JOHN ARGALL, III, KEVIN HOAGLAND-HANSON, JESSICA BODGER RYDSTROM, JESSICA PALMER RYEN; DOUGLAS ALEXANDER BEHRENS, GARY RUBMAN, CHRISTOPHER NEIL SIPES, Covington & Burling LLP, Washington, DC.

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DAVID LEE ANSTAETT, EMILY JANE GREB; DAN L. BAGATELL, Hanover, NH; SHANNON BLOODWORTH, NATHAN K. KELLEY, Washington, DC; VINNY LEE, Viatris Inc., Canonsburg, PA.

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

Opinion for the court filed by *Circuit Judge* STOLL.

Opinion dissenting in part filed by *Circuit Judge* TARANTO.

STOLL, *Circuit Judge*.

AstraZeneca AB and AstraZeneca Pharmaceuticals LP (collectively, "AstraZeneca") sued Mylan Pharmaceuticals Inc. and Kindeva Drug Delivery L.P. (collectively, "Mylan") for infringement of all claims of U.S. Patent Nos. 7,759,328; 8,143,239; and 8,575,137 (collectively, the "asserted patents"). After claim construction, Mylan stipulated to infringement and the district court entered judgment accordingly. The district court thereafter held a bench trial on invalidity and determined that Mylan failed to prove by clear and convincing evidence that the asserted claims are invalid as obvious. Mylan appeals from the stipulated judgment of infringement and the final judgment of no invalidity. First, Mylan challenges the district court's claim construction of "0.001%," the claimed amount of the excipient PVP, on which the stipulated judgment of infringement was based. For the reasons below, we disagree with the district court's construction and therefore vacate the judgment of infringement and remand. Second, Mylan challenges several factual findings underlying the district court's determination of nonobviousness. Because we discern no clear error in the district court's finding that the prior art taught away from the claimed invention, we affirm the determination of nonobviousness.

BACKGROUND

I

All of the asserted patents are listed in the U.S Food and Drug Administration's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book, as covering AstraZeneca's Symbicort® pressurized metered-dose inhaler (pMDI). The Symbicort® pMDI is approved for the treatment of asthma and chronic obstructive pulmonary disease (COPD). AstraZeneca has marketed a dry powder inhaler version of Symbicort® (Symbicort® Turbuhaler) since the early 1990s. Both the Symbicort® pMDI and the Symbicort® Turbuhaler administer two active ingredients to the lungs—formoterol, a bronchodilator that opens the airway, and budesonide, a steroid that reduces inflammation in the lungs.

A dry powder inhaler, as its name suggests, is a powder formulation that requires a patient to take a deep, fast breath to properly inhale the medication. This type of treatment has drawbacks for young children and elderly patients who may have trouble taking a deep enough breath to deliver the medication to the lower part of the lungs, which is often done in emergency situations when a patient is having trouble breathing, making it difficult for the patient to take a deep breath in the first place. A formulation administered using a pMDI, by contrast, uses a propellant gas that is in liquid form when under pressure in the pMDI device. When the patient activates the pMDI device by pressing down on a button, the propellant causes the medication to come out as a spray, much like an aerosol can. This type of delivery side steps the need for a patient to take a deep breath to get the medication fully into the lungs—"all the work is done for [the patient] by the gas that's been liquefied." J.A. 9558 (Trial Tr. 107:6–11). This makes it easier for children and elderly patients to take the medication.

The asserted patents reflect the work of the inventors to develop a stable formoterol/budesonide composition for administration via a pMDI. The claims are directed to pharmaceutical compositions comprising formoterol fumarate dihydrate and budesonide, as well as a number of inactive ingredients at specified concentrations. The inactive ingredients include HFA 227 (a propellant), PVP K25 (a formulation stabilizer), and PEG-1000 (a lubricant). Claim 13 of the '328 patent is representative of the claims on appeal and recites:

> 13. A pharmaceutical composition[1] comprising formoterol fumarate dihydrate, budesonide, HFA227, PVP K25, and PEG-1000, wherein the formoterol fumarate dihydrate is present at a concentration of 0.09 mg/ml, the budesonide is present at a concentration of 2 mg/ml, *the PVP K25 is present at a concentration of 0.001% w/w*, and the PEG-1000 is present at a concentration of 0.3% w/w.

'328 patent col. 8 ll. 58–64 (emphasis added to disputed limitation).

II

3M Company submitted Abbreviated New Drug Application (ANDA) No. 211699 to the FDA, seeking approval to manufacture and sell a generic version of the Symbicort® pMDI. Certain interests in ANDA No. 211699 were later transferred to Mylan. After those interests were transferred, Mylan notified AstraZeneca via a Paragraph IV letter that it had submitted ANDA No. 211699 for a generic

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[1] The parties agree that the term "pharmaceutical composition" means "suspension for therapeutic administration." In a suspension, the active ingredient remains as a solid in the liquid, whereas in a solution, the active ingredient would dissolve in the liquid.

version of the Symbicort® pMDI (Mylan's ANDA Product). Mylan's Paragraph IV letter argued that the asserted patents are invalid, unenforceable, and/or not infringed. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV). On October 12, 2018, AstraZeneca sued Mylan for infringement under 35 U.S.C. § 271(e)(2) based on Mylan's submission of ANDA No. 211699 seeking approval for its ANDA Product.

Not long before trial, the district court held a claim construction hearing to settle a late-arising dispute between the parties concerning the construction of "0.001%," the claimed concentration of PVP. Although the parties had originally agreed that no construction of this term was necessary, the dispute became apparent during briefing on Mylan's motion for partial summary judgment of noninfringement under the doctrine of equivalents. The district court construed "0.001%" according to its "plain and ordinary meaning, that is, expressed with one significant digit." *AstraZeneca AB v. Mylan Pharms. Inc.*, Civil Action No. 1:18CV193 c/w 1:19CV203, 2020 WL 4670401, at *7 (N.D. W. Va. Aug. 12, 2020). Mylan thereafter stipulated to infringement of certain claims of the asserted patents and the district court entered final judgment of infringement.

The district court then held a bench trial on validity of the asserted claims. The district court determined that Mylan failed to prove by clear and convincing evidence that the asserted claims would have been obvious in view of the prior art and entered a final judgment of no invalidity. *AstraZeneca AB v. Mylan Pharms. Inc.*, 522 F. Supp. 3d 200 (N.D. W. Va. Mar. 2, 2021) (*Judgment Op.*). The district court's ultimate determination was based on several underlying factual findings, including a finding that one of the prior art references Mylan relied on in its obviousness

combination, Rogueda,[2] taught away from the claimed invention. *Id.* at 219–20.

Mylan appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

On appeal, Mylan challenges the district court's construction of "0.001%," the claimed concentration of PVP. Mylan also challenges several of the factual findings underlying the district court's nonobviousness determination, including its finding that the prior art taught away from the claimed invention. We address each issue in turn.

I

We begin with Mylan's challenge to the district court's construction of "0.001%," the claimed concentration of PVP. Our review of the district court's claim construction is de novo where, as here, it is decided only on the intrinsic evidence. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 331 (2015).

The question here is whether the concentration of PVP being "0.001%" means 0.001% within one significant figure—encompassing a concentration of PVP in the range of 0.0005% to 0.0014%, as AstraZeneca contends and as the district court construed this term—or it has a narrower meaning in view of the specification and the prosecution history—precisely 0.001% w/w PVP with only "minor variations," as Mylan contends. This is a close call. Ultimately, for the reasons below, we conclude that Mylan's proposed construction, albeit articulated differently, is correct because it "most naturally aligns with the patent's description of the invention," as further informed by the prosecution history. *Takeda Pharm. Co. Ltd. v. Zydus Pharms. USA, Inc.*, 743 F.3d 1359, 1363 (Fed. Cir. 2014)

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[2] PCT Pub. No. WO 2002/03958.

(quoting *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998)). We therefore construe "0.001%" as that precise number, with only minor variations, i.e., 0.00095% to 0.00104%.

We begin, as we must, with the claim language itself. The parties agree that the term "0.001%," being expressed using only a single significant figure, would ordinarily, as an abstract number on a page, encompass a range from 0.0005% to 0.0014%. Oral Arg. at 14:18–15:15, 21:48–22:22, http://oralarguments.cafc.uscourts.gov/default.aspx?fl=21-1729_08312021.mp3. This is a standard scientific convention, and numbers falling within that range would typically be rounded up or down to 0.001%. AstraZeneca argues that this "ordinary meaning" controls absent lexicography or disclaimer. Appellees' Br. 39 (first citing *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1369 (Fed. Cir. 2012); and then citing *Thorner v. Sony Comput. Ent. Am.*, 669 F.3d 1362, 1365–67 (Fed. Cir. 2012)). We disagree, as this narrow view of our precedent would necessitate adopting an acontextual construction of this disputed claim term, improperly isolating the numerical term from the more complete term "PVP K25 is present at a concentration of 0.001% w/w," as well as the specification and prosecution history descriptions of PVP concentrations.

Indeed, as we have explained, the "ordinary meaning of a claim term is not 'the meaning of the term in the abstract.' . . . Instead, 'the "ordinary meaning"' of a claim term is its meaning to the ordinary artisan after reading the entire patent.'" *Eon Corp. IP Holdings v. Silver Spring Networks*, 815 F.3d 1314, 1320 (Fed. Cir. 2016) (quoting *Phillips v. AWH Corp.*, 415 F.3d 1303, 1321 (Fed. Cir. 2005) (en banc)); *see also Trs. of Columbia Univ. v. Symantec Corp.*, 811 F.3d 1359, 1363 (Fed. Cir. 2016) ("The only meaning that matters in claim construction is the meaning in the context of the patent."). Consistent with *Phillips*, therefore, we must read the claims in view of both the written description and prosecution history. 415 F.3d at 1315,

1317; *Eon*, 815 F.3d at 1320 ("A party is . . . 'not entitled to a claim construction divorced from the context of the written description and prosecution history.'" (quoting *Nystrom v. TREX Co.*, 424 F.3d 1136, 1144–45 (Fed. Cir. 2005))); *Ultimate Pointer, L.L.C. v. Nintendo Co.*, 816 F.3d 816, 823–24 (Fed. Cir. 2016) (rejecting patentee's proposed "ordinary meaning" construction because it was divorced from "the repeated direct-pointing description and indirect-pointing criticism in the specification"). As we explain in detail below, both the written description and prosecution history place considerable emphasis on the stability of the claimed formulations, i.e., formulations with 0.001% w/w PVP, compared to formulations with slightly higher or slightly lower concentrations of PVP, including for example, 0.0005% w/w. Thus, taken as a whole, the intrinsic record supports a narrower construction of 0.001% to reflect that term's application to the PVP concentration in particular, and the testing evidence in the written description and prosecution history showing that very minor differences in the concentration of PVP—down to the ten-thousandth of a percentage (fourth decimal place)—impact stability.

We turn first to the written description—which "is always highly relevant to the claim construction analysis" and indeed is often "the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). According to the written description, "[s]tability is one of the most important factors which determines whether a compound or a mixture of compounds can be developed into a therapeutically useful pharmaceutical product." '328 patent col. 1 ll. 21–24. The inventors discovered that "certain HFA formulations comprising formoterol and budesonide together with" PVP and PEG "exhibit excellent physical suspension stability." *Id.* at col. 1 ll. 32–35. Specifically, the written description explains that "[t]he concentration of PVP (0.001% w/w) used in this

formulation has been found to give consistently stable formulations over the required dose range." *Id.* at col. 2 ll. 17–21. And the written description repeatedly touts the superior stability of formulations with 0.001% w/w PVP. *See, e.g.*, *id.* at col. 6 ll. 30–31 ("formulations with 0.001% w/w PVP gave the best suspension stability overall"), ll. 40–42 ("the formulation containing 0.001% PVP is the most stable"), ll. 49–51 ("the most stable formulation is . . . with 0.001% w/w PVP"), ll. 52–54 ("the suspension with 0.001% w/w PVP is the most stable").

The inventors' conclusion that formulations with 0.001% w/w PVP are the "most stable" is evidenced by the data they provided in the specification. As part of their experiments, the inventors tested formulations including PVP at concentrations of 0.0001%, 0.0005%, 0.001%, 0.01%, 0.03%, and 0.05% w/w and characterized each formulation for stability. Figures 3 and 5 provide stability results for 80 μg budesonide formulations, which corresponds to the claimed 2 mg/mL budesonide concentration. Figure

3 provides stability results for these formulations based on OSCAR[3] data:

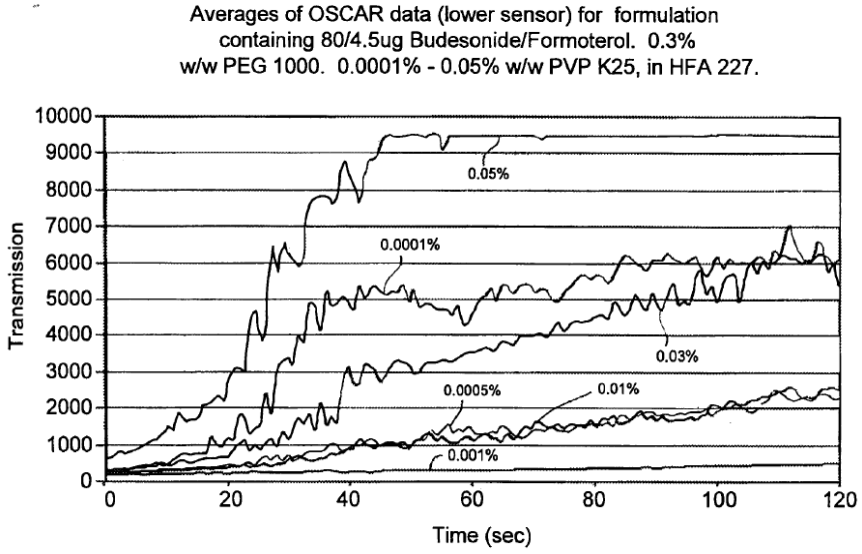

FIG. 3

Id. Fig. 3. In Figure 3, "the bottom line, . . . with low transmission readings, clearly shows that the formulation containing 0.001% PVP is the most stable." *Id.* at col. 6 ll. 40–42. As shown above, the formulation with 0.001% w/w PVP has a lower transmission measurement than the formulation with 0.0005% w/w PVP, meaning the formulation with 0.001% w/w PVP is more stable than the 0.0005% w/w PVP formulation. The Turbiscan[4] data provided in Figure 5 is even more significant, showing that the

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[3] OSCAR refers to "Optical Suspension Characterization" equipment, which "utili[z]es changes in light transmission with time, to characteri[z]e a pre-agitated suspension formulation." *Id.* col. 3 ll. 10–16.

[4] Turbiscan analyzers are "concentrated dispersion and emulsion stability and instability analy[z]ers" that characterize sample "homogeneity, concentration[,] and mean particle diameter." *Id.* at col. 3 ll. 48–50, ll. 62–65.

formulation comprising 0.0005% w/w PVP (second from the top) was one of the least stable formulations tested:

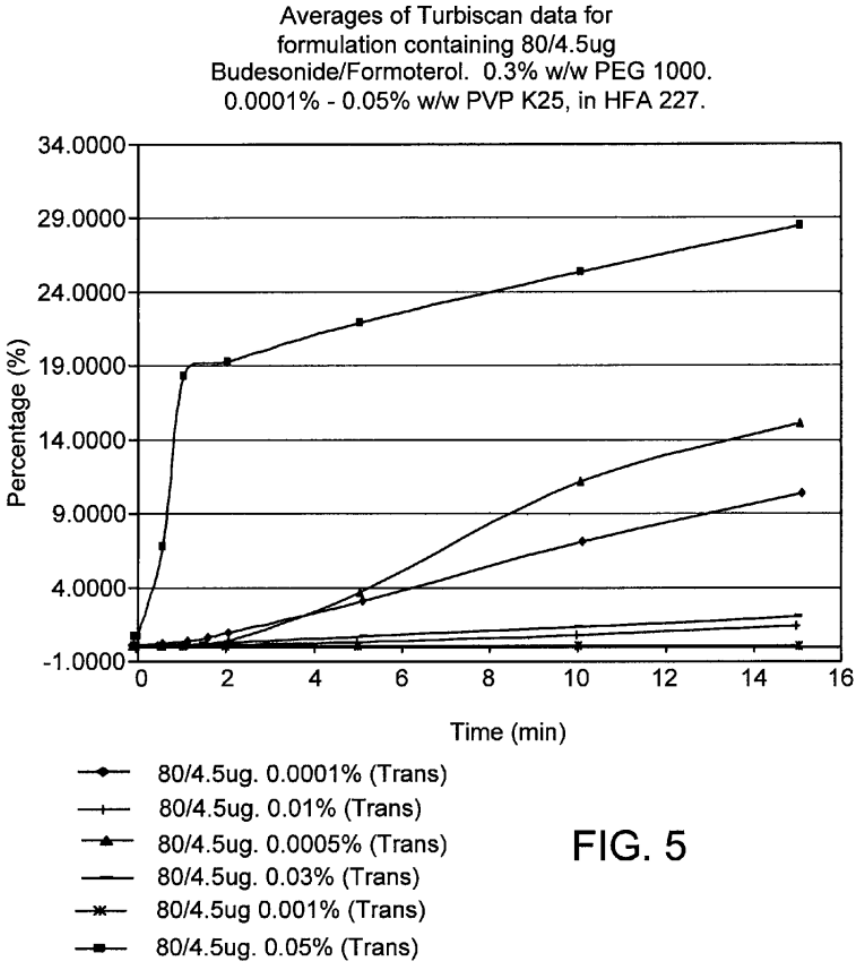

FIG. 5

Id. Fig. 5. Consistent with the OSCAR data, "the suspension with 0.001% w/w PVP is the most stable (bottom bold line)" of the formulations tested. *Id.* at col. 6 ll. 52–54.

Based on the written description, it is clear that the inventors understood that a formulation comprising 0.001% w/w PVP is more stable than (and indeed, different from) a formulation with even a slight difference in the concentration of PVP, *e.g.*, a formulation with 0.0005% w/w PVP. This data leaves little room for doubt that slight

differences in the concentration of PVP—down to the ten-thousandth of a percentage (fourth decimal place)—matters for stability in the context of this invention. Thus, while an acontextual read of the term 0.001% might encompass amounts of an excipient or active ingredient between 0.0005% and 0.0014%, the written description suggests that the claimed formulations with 0.001% w/w PVP were intended to be more exact. The construction we adopt today, which allows for only minor variations in the PVP concentration at the fourth decimal place (0.00095% to 0.00104%), reflects the level of exactness the inventors used in the written description in concluding that 0.001% w/w PVP is the most stable formulation compared to formulations with slightly more or less PVP.

This construction is also supported by the prosecution history, which "often inform[s] the meaning of the claim language by demonstrating how the inventor understood the invention." *Phillips*, 415 F.3d at 1317. The original version of claim 2 that was filed in the application that led to the '328 patent recited a PVP concentration "from about 0.0005 to about 0.05 %w/w." J.A. 15919. The Examiner rejected the claims as obvious over two prior art references of record, explaining that "one would have been expected to determine the optimum amount of PVP." J.A. 16205. The inventors then amended the claims, deleting the PVP range limitation from claim 2 in its entirety and amending claim 1 to recite that the "PVP is present in an amount of 0.001% w/w." J.A. 16213. This amendment narrowed the scope of claim 1, which previously did not recite any PVP concentration, by limiting the amount of PVP to 0.001% w/w without using the "about" qualifier that had been previously included in claim 2. The inventors argued, in support of their proposed claim amendment, that they had "surprisingly demonstrated that 0.001% w/w PVP gave the best suspension stability when compared to a range of PVP concentrations from 0.0001% to 0.05% w/w." J.A. 16222.

The Examiner once again rejected the claims, stating that it was "imperative" for the inventors to show "criticality of the invention comprising 0.001% w/w PVP by testing the invention comprising *slightly more and less* than 0.001% w/w PVP." J.A. 16307 (emphasis added); *id.* ("Applicant fails to provide examples, which show the criticality of 0.001% w/w PVP versus the invention where the PVP concentration is slightly greater or less than 0.001% w/w PVP."). In response, the inventors asserted that the "criticality of 0.001% w/w PVP in a formulation containing 2 mg/ml budesonide" was illustrated by the data provided in the written description—specifically, Figures 3 and 5—which compared the stability of a 0.001% w/w PVP formulation to formulations with 0.0001%, 0.0005%, 0.01%, 0.03%, and 0.05% w/w PVP. J.A. 16326; *see also* '328 patent Figs. 3, 5. The inventors further claimed that

> formulations with *higher or lower concentrations of PVP* were less able to maintain a good suspension of a 2 mg/ml budesonide formulation over time. Nothing in the prior art would have led one to expect that 0.001% w/w PVP would provide this benefit in a formulation containing 2 mg/ml budesonide (or any other concentration of budesonide, for that matter).

J.A. 16326–27 (emphasis added).

At this time, the inventors once again sought to obtain claims reciting a variety of different PVP concentrations, including "0.001% w/w to 0.01% w/w" PVP (claim 1), "0.0001% to 0.001% w/w" PVP (claim 18), and "0.0001%, 0.0005%, or 0.001% w/w" PVP (claim 23). J.A. 16319–21. For claims specifically directed to 2 mg/mL budesonide formulations (the claimed concentration of budesonide in the asserted claims), however, the inventors only sought claims specifying "0.001% w/w" PVP, J.A. 16320 (claim 16), consistent with their assertion that 0.001% w/w PVP was critical for stability of a 2 mg/mL budesonide formulation.

After the Examiner rejected the claims because they were "not commensurate in scope with the unexpected results" that the inventors presented, J.A. 16447, AstraZeneca canceled these claims, narrowed a previously presented claim to recite a PVP concentration of 0.001% w/w, J.A. 16455 (claim 25), and introduced several new claims that, likewise, recited a PVP concentration of exactly 0.001% w/w, J.A. 16456–57 (claims 45–48) including formulations with 2 mg/mL budesonide, *id.* (claim 46). The Examiner ultimately allowed the claims, stating in the reasons for allowance that the "results provided in the specification . . . for the stability of the instant composition overcomes any obviousness type rejection that could have been deduced from" the prior art of record. J.A. 16479.

Over the course of the prosecution history, the inventors narrowed the claimed concentration of PVP to 0.001% w/w from a broader range without using the qualifier "about." The inventors did this not just once but multiple times, each time emphasizing to the Examiner that 0.001% w/w PVP—not concentrations slightly more or less than 0.001% w/w—was critical to stability of the claimed 2 mg/mL budesonide formulation. And, importantly, the prosecution history shows that the inventors knew how to claim ranges or describe numbers with approximation, e.g., by using the term "about" to qualify the amount of PVP claimed. Yet, in the asserted claims, the inventors chose to claim exactly 0.001% w/w PVP. Under our precedent, this provides further support for construing 0.001% narrowly. *See, e.g.*, *Takeda*, 743 F.3d at 1365 (rejecting district court's construction of "400 μm" that permitted a 10% margin of error in the particle size measurement where the intrinsic record demonstrated the inventors knew to use the term "about" in claim language to allow for margin of error in numerical measurements but chose not to use "about" in the disputed claim term). Indeed, the public should reasonably be able to rely on these amendments and

arguments in the prosecution history to inform the scope of the claimed invention.

We recognize that, as the parties agreed, there needs to be some room for experimental error in the PVP concentration. The construction we adopt today reflects a margin of error that is best supported by the intrinsic record. This construction, which allows for only minor variations in the PVP concentration at the fourth decimal place, representing a 5% variation in the PVP concentration—as opposed to AstraZeneca's, which would allow up to a 50% variation in the PVP concentration—more accurately reflects the level of exactness the inventors used in the written description in concluding that 0.001% w/w PVP is the most stable formulation, as well as the arguments and amendments in the prosecution history asserting that 0.001% w/w PVP is "critical" compared to formulations with slightly more or less PVP.

We are not persuaded by AstraZeneca's arguments to the contrary. AstraZeneca first argues that the written description and prosecution history only ever express the PVP concentration with one significant figure, whereas the concentration of some of the other ingredients, e.g., budesonide, are expressed using additional significant figures. Appellees' Br. 34–35; *see also* '328 patent col. 7 ll. 62–65. Thus, according to AstraZeneca, adopting Mylan's proposed construction would effectively make the concentration of PVP more precise than the inventors intended, because the inventors could have used additional significant figures to reflect the need for greater precision with the concentration of PVP. In light of the specification and prosecution history, we disagree. Though true that the inventors expressed the concentration of PVP using a single significant figure throughout the written description, this fact does not dictate the result that AstraZeneca seeks. As explained above, the written description repeatedly differentiates between formulations comprising 0.001% w/w PVP and, e.g., those comprising 0.0005% w/w PVP,

emphasizing that the level of precision required in the context of this invention with respect to the concentration of PVP is down to the ten-thousandth of a percentage. AstraZeneca's proposed construction ignores that context.

AstraZeneca also argues that Mylan's proposed construction is an impermissible attempt to limit the scope of the claims to the preferred embodiment. Appellees' Br. 40–41. We are not persuaded. We are, of course, mindful not to limit claims to their preferred embodiments. But AstraZeneca's proposed construction would read on two distinct formulations described in the written description—namely, a formulation comprising 0.0005% w/w PVP and one comprising 0.001% w/w PVP. Yet, the inventors chose to claim only one of these formulations, which supports construing the claims as limited to that formulation. Second, we have explained that "during prosecution, an applicant may have cancelled pending claims but not amended the specification to delete disclosure relevant only to the cancelled claims. In such cases, unasserted or cancelled claims may provide 'probative evidence' that an embodiment is not within the scope of an asserted claim." *PSN Ill., LLC v. Ivoclar Vivadent, Inc.*, 525 F.3d 1159, 1166 (Fed. Cir. 2008). Such is the case here. The inventors previously included claims covering alternative embodiments described in the written description—including claims to formulations with 0.0005% w/w PVP. That the inventors later canceled these claims provides further evidence that formulations with 0.0005% w/w PVP are not within the scope of the claims at issue here.

Nor do we agree with AstraZeneca that the prosecution history is irrelevant because there is no clear and unmistakable disavowal of claim scope. Appellees' Br. 39, 45–46. We have stated that "[a]ny 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." *Fenner Invs., Ltd.*

v. Cellco P'ship, 778 F.3d 1320, 1323 (Fed. Cir. 2015) (quoting *Retractable Techs., Inc. v. Becton, Dickinson & Co.*, 653 F.3d 1296, 1305 (Fed. Cir. 2011)). "Accordingly, even in the absence of a clear and unmistakable disavowal, . . . the prosecution history can be evaluated to determine how a person of ordinary skill would understand a given claim term." *Aptalis Pharmatech, Inc. v. Apotex Inc.*, 718 F. App'x 965, 971 (Fed. Cir. 2018).

* * *

Although the term "0.001%" without any broader context might indicate a range from 0.0005% to 0.0014%, here, in the context of the concentration of PVP, in light of the testing data in the specification and the amendments and arguments in the prosecution history, we conclude that the construction of this term most consistent with the intrinsic evidence is not so broad. Accordingly, we construe "0.001%" as that precise number, with only minor variations, i.e., 0.00095% to 0.00104%. We therefore vacate the stipulated judgment of infringement and remand for the district court to find in the first instance whether Mylan's ANDA Product infringes the asserted claims under the proper claim construction.

II

We turn next to Mylan's challenge to the district court's nonobviousness determination. Following a bench trial, we review the district court's legal determinations de novo and its factual findings for clear error. *See Merck Sharp & Dohme Corp. v. Hospira Inc.*, 874 F.3d 724, 728 (Fed. Cir. 2017). "A factual finding is only clearly erroneous if . . . we are left with the definite and firm conviction that a mistake has been made." *Id.* "Obviousness is a question of law based on underlying findings of fact." *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1382 (Fed. Cir. 2019) (quoting *In re Kubin*, 561 F.3d 1351, 1355 (Fed. Cir. 2009)). "What the prior art teaches, whether a person of ordinary skill in the art would have been motivated to combine

references, and whether a reference teaches away from the claimed invention are questions of fact." *Meiresonne v. Google, Inc.*, 849 F.3d 1379, 1382 (Fed. Cir. 2017) (citing *Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1047–48 (Fed. Cir. 2016) (en banc)).

Mylan argues on appeal that several factual findings underlying the district court's nonobviousness determination are clearly erroneous, including its finding that the prior art reference Rogueda taught away from the claimed invention. Because we discern no clear error in the district court's teaching away finding, which on its own is sufficient to sustain the nonobviousness determination, we affirm.

Rogueda is a PCT publication that is directed to "stable pharmaceutical aerosol formulation[s] intended for inhalation." Rogueda, Abstract. Rogueda's novel formulations are suspensions "contain[ing] an active substance, an aerosol propellant, a polar fluorinated molecule and an excipient," with the "preferred propellant" being "HFA 134a or HFA 227 or a mixture thereof." *Id.* In the course of developing these novel formulations, Rogueda prepared certain control formulations to compare its novel formulations to. Mylan relied on two of these control formulations—specifically, control formulations 3 and 9—as rendering obvious the claimed formulations. The table below summarizes the components of the control formulations as well as representative claim 13 of the '328 patent.

Component	*Claim 13*	*Control 3*	*Control 9*
Formoterol Fumarate Dihydrate	0.09 mg/mL	0.0167% w/w (0.16 mg/mL)	No
Budesonide	2 mg/mL	No	0.259% w/w (2.59 mg/mL)
PVP K25	0.001% w/w	0.001% w/w	0.001% w/w
PEG-1000	0.3% w/w	0.1% w/w	0.3% w/w
HFA227	Yes	Yes	Yes

See id. at p. 24 l. 16–p. 25 l. 5, p. 25 ll. 29–33; '328 patent col. 8 ll. 58–64.

Rogueda conducted a number of studies to characterize its novel formulations as compared with the control formulations. These tests included monitoring the extent of drug adhesion to the dispensing device, the extent to which the formulations creamed (which refers to whether the active ingredient floated out of the suspension, much like curdled milk), and an evaluation of the particle size. With respect to adhesion to the dispensing device, Rogueda concluded that both the budesonide and formoterol novel formulations exhibited a "drastic[]" reduction in the amount of drug adhesion compared to their controls (controls 9 and 3, respectively). Rogueda p. 27 ll. 25–38. AstraZeneca's expert Dr. Paul M. Young testified that a skilled artisan looking at the adhesion test results in Rogueda would conclude that the control formulations "were not suitable" and "clearly don't work." J.A. 10152–53 (Trial Tr. 684:3–6, 685:8–14); *see also* J.A. 10148–54 (Trial Tr. 680:1–686:21). Dr. Young also testified that a skilled artisan, therefore, would not have used the control formulations as a starting

point for optimization or experimentation given the poor adhesion results reported in Rogueda. J.A. 10154 (Trial. Tr. 686:18–21).

With respect to the particle size, Rogueda concluded that the novel formulations had a narrower size distribution and smaller average particle size than the control formulations, noting that the particles in the novel formulations existed as "individual particles and not as clusters." Rogueda p. 30 ll. 9–12; *see also id.* at pp. 29–31. Dr. Young testified that, for the novel formulations, the particle size reported by Rogueda "is a suitable size for inhalation." J.A. 10162 (Trial Tr. 694:17–18). By contrast, for the control formulations, Dr. Young explained that the particle size reported by Rogueda was significantly larger, indicating that there were "huge agglomerates . . . floating around" in the formulations, rendering them "completely unsuitable." J.A. 10162–63 (Trial Tr. 694:24–695:8). Considering Rogueda's data in its entirety, Dr. Young testified that a skilled artisan would consider the control formulations "just unsuitable," and therefore would not have any reason to use these control formulations as a basis for experimentation. J.A. 10164 (Trial Tr. 696:7–18).

Under this court's precedent, a prior art reference is said to teach away from the claimed invention if a skilled artisan "'upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken' in the claim." *Meiresonne*, 849 F.3d at 1382 (quoting *Galderma Lab'ys, L.P. v. Tolmar, Inc.*, 737 F.3d 731, 738 (Fed. Cir. 2013)). And a "reference that properly teaches away can preclude a determination that the reference renders a claim obvious." *In re Mouttet*, 686 F.3d 1322, 1333 (Fed. Cir. 2012). The district court, applying this standard, credited Dr. Young's testimony discussed above in finding that a skilled artisan "would have been discouraged from incorporating the formulations in Controls 3 and 9" because "the data cut against the very goal a [skilled artisan]

would have been trying to achieve—a stable product with a consistent dose." *Judgment Op.*, 522 F. Supp. 3d at 219–20. The district court concluded, therefore, that "Rogueda teaches away and does not render the claims obvious." *Id.* at 220. We discern no clear error in this finding and therefore affirm the district court's determination of nonobviousness.

We are unpersuaded by Mylan's arguments that Rogueda does not teach away. Mylan first argues that the district court's finding is contrary to this court's precedent, which holds that a reference that "'merely expresses a general preference for an alternative invention but does not criticize, discredit, or otherwise discourage investigation into' the claimed invention does not teach away." *Meiresonne*, 849 F.3d at 1382 (quoting *Galderma*, 737 F.3d at 738). Specifically, Mylan points to a one-off sentence in the district court's opinion—stating that "Rogueda did not necessarily disparage the formulations in Controls 3 and 9," *Judgment Op.*, 522 F. Supp. 3d at 219–20—as supporting the notion that Rogueda merely expresses a preference for the novel formulations over the control formulations. Appellants' Br. 57. We disagree. Although true Rogueda itself does not contain explicit disparagement of the control formulations, the district court properly relied on expert testimony regarding how a skilled artisan would interpret the data in Rogueda to find implicit disparagement. Indeed, whether a reference teaches away must be determined from the viewpoint of a skilled artisan. And, as discussed above, the district court credited Dr. Young's testimony that a person of ordinary skill in the art would have known that the control formulations were unsuitable for further experimentation, thus "discouraging investigation into" these formulations.

Mylan's remaining arguments amount to no more than asking us to reweigh the evidence on appeal. For instance, Mylan argues that the control formulations "were stable during the critical seconds after shaking." Appellants'

Br. 59. It also argues that there were known solutions to can adhesion and particle aggregation and, therefore, the problems Dr. Young discussed with respect to the control formulations were not real problems. *Id.* at 60–61. The district court, sitting as fact finder, considered this testimony and nevertheless found that a skilled artisan would have been discouraged from using Rogueda's control formulations as a basis for further experimentation. Absent clear error, we will not disturb the district court's weighing of the evidence on appeal.

CONCLUSION

We have considered the parties' remaining arguments and find them unpersuasive. Because we conclude that the district court erred in its claim construction, we vacate the stipulated judgment of infringement and remand for further proceedings on infringement consistent with our claim construction. We also conclude that the district court did not clearly err in finding the prior art taught away from the claimed invention and therefore affirm the judgment of no invalidity.

AFFIRMED-IN-PART, VACATED-IN-PART, AND REMANDED

COSTS

No costs.

United States Court of Appeals for the Federal Circuit

ASTRAZENECA AB, ASTRAZENECA PHARMACEUTICALS LP,
Plaintiffs-Appellees

v.

MYLAN PHARMACEUTICALS INC., KINDEVA DRUG DELIVERY L.P.,
Defendants-Appellants

2021-1729

Appeal from the United States District Court for the Northern District of West Virginia in No. 1:18-cv-00193-IMK-RWT, 1:19-cv-00203-IMK, Judge Irene M. Keeley.

TARANTO, *Circuit Judge*, dissenting in part.

I join the Background section of the court's opinion and part II of the Discussion section, which affirms the district court's rejection of Mylan's obviousness challenge. But I do not join part I of the Discussion section, which addresses a dispute over claim construction pertinent to the judgment of infringement. In that section, the court holds that, in claims reciting a concentration of "0.001% w/w" (weight per weight) of a particular suspension agent in the claimed composition, the term "0.001%" should not be construed (as the district court construed it) to have its conventional significant-figure meaning, but, instead, to mean "that precise

number, with only minor variations"—which the court then equates to what the term would mean if it were rewritten as "0.0010%" (adding an extra significant figure). I respectfully dissent from that holding.

In my view, "0.001%" should be construed to have its significant-figure meaning, *i.e.*, the interval 0.0005% to 0.0014%, as the district court held, with only one possible interval-shrinking change that cannot matter in this case. The possible change is to exclude those concentration levels which are in the overlap area between the significant-figure interval of "0.001%" and the significant-figure interval of "0.0005%" (*i.e.,* 0.00045% to 0.00054%), another concentration level addressed separately in the patent's testing description. If that exclusion were adopted, the language as construed would cover the interval 0.00055% to 0.0014%. But we need not resolve whether the exclusion of the overlap of the two significant-figure intervals is actually a proper part of the construction, because a finding of infringement is compelled regardless.

I

A

AstraZeneca owns U.S. Patent Nos. 7,759,328, 8,143,239, and 8,575,137, which share a specification, and AstraZeneca was the assignee during prosecution. The patents describe and claim a suspension composition in a pressurized metered dose inhaler (pMDI) for the treatment of asthma and other respiratory diseases. '328 patent, col. 1, lines 14–35; *id.*, col. 8, line 16, through col. 10, line 5. The composition, characterized by five specified components, contains two active ingredients (budesonide and formoterol), a propellant (an HFA, *i.e.*, heptafluoropropane), and two excipients (PVP, *i.e.*, polyvinylpyrrolidone; and PEG, *i.e.*, polyethylene glycol). *Id.*, col. 8, lines 17–26. The '328 patent claims particular grades of the two excipients (PVP K25 and PEG-1000) by concentration in units of weight percent (% w/w). The PVP K25 functions as a

suspension agent. Claim 13 of the '328 patent, which all parties have treated as representative for claim-construction purposes, reads:

> A pharmaceutical composition comprising formoterol fumarate dihydrate, budesonide, HFA 227, PVP K25, and PEG-1000,
>
> wherein the formoterol fumarate dihydrate is present at a concentration of 0.09 mg/ml,
>
> the budesonide is present at a concentration of 2 mg/ml,
>
> the PVP K25 is present at a concentration of 0.001% w/w,
>
> and the PEG-1000 is present at a concentration of 0.3% w/w.

Id., col. 8, lines 58–64.

The limitation in dispute in the representative claim states the concentration of the PVP excipient: "the PVP K25 is present at a concentration of 0.001% w/w." *Id.*, col 8, lines 62–63. The '137 and '239 patents claim concentration ranges of excipients, and only some claims claim a particular grade of each excipient. Both require a range defined in part by "0.001%": "the PVP is present at a concentration in the range of 0.001% to 0.01% w/w." *See* '137 patent, col. 8, lines 22–23; '239 patent, col. 9, lines 1–2.

The specification discusses testing of the suspension stability of various five-component formulations. *See* '328 patent, col. 5, line 28, through col. 6, line 28. The specification describes formulations with varying PVP concentrations and those formulations' assessed stability. *Id.*, col. 5, line 60, through col. 6, line 31. The six concentrations of PVP tested are reported as "0.0001%," "0.0005%," "0.001%," "0.01%," "0.03%," and "0.05%" w/w. *Id.* The specification states that several of those formulations were "considered excellent," *id.*, col. 6, line 29, and formulations

with "0.001%" w/w PVP "gave the best suspension ability overall," *id.*, col. 6, lines 30–31.

In AstraZeneca's initial application for what became the '328 patent, original claim 1 recited the five-component composition with no concentration limitations, while several dependent claims contained such limitations, including one claiming PVP "present from about 0.0005 to about 0.05 %w/w" and a PEG concentration range. J.A. 15919. The examiner rejected the claims for obviousness over two references (U.S. Patent Appl. Publ. No. 2003/0018019 to Meade and U.S. Patent No. 6,309,623 to Weers). J.A. 16204–05. The examiner listed several bases for the rejection, including that "one would have been expected to determine the optimum amount of PVP and PEG (which may have fallen within the [claimed] range)." J.A. 16205.

AstraZeneca then amended its claim 1 to include a concentration of the claimed PVP (but none of the four other components), stating: "PVP is present in an amount of 0.001% w/w." J.A. 16213. In support of allowance, AstraZeneca argued that neither prior-art reference disclosed a PVP concentration. AstraZeneca identified a reference (U.S. Patent No. 6,123,924 to Mistry) that, it observed, disclosed concentrations of PVP notably higher than its newly claimed "0.001%," *i.e.*, the reference disclosed concentrations from "0.0025%" to "0.5% w/w." J.A. 16222. AstraZeneca argued that it had made the "surprising discovery" that "0.001%" PVP gave "consistently stable formulations . . . at a much lower concentration than indicated in the prior art." J.A. 16222 (internal quotation marks and citation omitted). After AstraZeneca's amendment, the examiner again rejected the claims, stating, as one ground, that neither Meade nor Weers "disclose[s] any particular range of PVP" and AstraZeneca "fails to provide examples, which show the criticality of 0.001 % w/w PVP versus the invention where the PVP concentration is slightly greater or less than 0.001 % w/w PVP." J.A. 16307; *see also* J.A. 16306.

On continued examination, AstraZeneca then cancelled some claims and submitted new and amended claims reciting, for different amounts of budesonide, several different concentrations and ranges of concentrations of PVP (in one claim for PVP K25 specifically) whose testing is described in the specification, from "0.0001%" to "0.01%" w/w. J.A. 16319–28. The examiner, however, issued another rejection for obviousness over the two references originally cited, noting that "[w]ith respect to the experimental results provided by the Applicants, the claims are much broader than what are being interpreted as unexpected results" and that the "specification states . . . that only 0.001% PVP is used in all formulations." J.A. 16447. AstraZeneca responded by cancelling some claims and submitting new and amended claims that added concentration levels or ranges for each component, including, now, a PVP concentration (in one claim for PVP K25 specifically) limited to "0.001%" w/w. J.A. 16455–57. AstraZeneca disclaimed any concession as to the scope of unexpected results, J.A. 16460, and also disagreed with the examiner's assertion that the specification states that "only 0.001% PVP is used in all formulations" but deemed that issue "moot in light of the current amendments," *id.* After the examiner suggested a narrowing of all PVP terms to PVP K25, and AstraZeneca agreed, the examiner allowed the claims, which issued with PVP K25 language as slightly modified after allowance.

AstraZeneca's subsequent continuation applications issued as the '239 and '137 patents, with claims reciting PVP (with some but not all claims limited to PVP K25) at concentration levels not limited to "0.001%" but including a range of "0.001% to 0.01% w/w." '239 patent, col. 8, line 61, through col. 10, line 48; '137 patent, col. 8, line 16, through col. 10, line 49.

B

After Mylan sought FDA approval of an Abbreviated New Drug Application and sent AstraZeneca a Paragraph IV Certification Notice Letter, J.A. 7034–82, AstraZeneca brought this Hatch-Waxman suit in the District of Delaware, asserting infringement of the '328, '239, and '137 patents. The parties exchanged proposed claim constructions for "0.001% w/w," a term that appeared in all asserted claims. Mylan proposed a construction of "0.0010% w/w," J.A. 7027, which added a zero at the end to create two significant figures. This was the same position Mylan took in its Notice Letter, which stated that the claim term had one meaning if left at one significant figure (as written) and another meaning if changed to two significant figures (as urged by Mylan), the interval defined by the latter being much smaller than the interval defined by the former. J.A. 7080–82.[1] AstraZeneca proposed that no construction was

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[1] In its Notice Letter, Mylan explained "significant figures" generally:

> The significant figures of a number are digits that carry meaning contributing to its measurement resolution. This includes all digits beginning with the first non-zero digit. That is, leading zeros are not significant figures regardless of whether or not a decimal point is present. Trailing zeros are always significant when a decimal point is present."

J.A. 7080 n.6 (citing http://ccnmtl.columbia.edu/projects/mmt/frontiers/web/chapter_5/6665.html). As to the claim phrase, "0.001% w/w PVP K25," Mylan wrote:

> The claim phrase "0.001% w/w PVP K25" is amenable to two potential constructions, based on the number of significant figures a person of ordinary skill in the art would accord the value 0.001% w/w. Were the person of ordinary skill to accord the

necessary. In the alternative, it proposed "0.001% w/w, expressed using one significant digit." J.A. 7013. "In an effort to streamline claim construction," Mylan then agreed that no construction was necessary for the PVP concentration terms. J.A. 5612; 12927 n.3.

The case was then transferred to the Northern District of West Virginia, where Mylan again asserted that the term "0.001%" required construction and requested additional briefing, a request that the court granted. AstraZeneca presented the same construction as it did in the Delaware court. But Mylan in its opening brief in West Virginia now argued for a new construction—the term "0.001%" meant "that precise number, with only minor variations." J.A. 6804. In its reply brief, however, Mylan equated that construction with its construction originally proposed in Delaware, J.A. 7708 ("Defendants' construction of '0.0010%' PVP permits minor concentration variations."), as it did in oral argument to the West Virginia court, J.A. 7913, 7915 (arguing that the term "requires two significant figures").

> value two significant figures, then the proper construction would be 0.0010% w/w PVP K25 and, it would follow, that rounding would literally encompass between 0.00095% and 0.00105% w/w PVP K25. Alternatively, were the person of ordinary skill to accord the value one significant figure, then the proper construction would be 0.001% w/w PVP K25, and it would follow that rounding would literally encompass between 0.0005% to 0.0014% w/w PVP K25. For the reasons set forth below, the phrase "0.001% w/w PVP K25" should be construed as having at least two significant figures, i.e., "0.0010% w/w PVP K25."

J.A. 7080–81 (citation to J.A. 7080 n.6 omitted).

The West Virginia district court "construe[d] the term '0.001%' consistent with its plain and ordinary meaning, that is, expressed with one significant digit." *AstraZeneca AB v. Mylan Pharms. Inc.*, No. 1:18-CV-193 c/w 1:19-CV-203, 2020 WL 4670401, at *7 (N.D. W. Va. Aug. 12, 2020). Based on the rules of rounding, the court determined that the plain meaning of the term "0.001%" encompassed the range of 0.0005% to 0.0014%. *Id.* at *5 (citing *Noven Pharms., Inc. v. Actavis Laboratories UT, Inc.*, C.A. No. 15-249-LPS, 2016 WL 3625541, at *3, 5 (D. Del. July 5, 2016)). The court found that neither the specification nor the prosecution history supported Mylan's construction. *Id.* at *5–6. Mylan stipulated to infringement under AstraZeneca's construction. The district court entered a final judgment of infringement.

II

A

"[T]he words of a claim are generally given their ordinary and customary meaning," as understood by a skilled artisan at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc) (citations and internal quotations omitted). It is undisputed that the term "0.001%" here, which states a concentration of a component, has an ordinary meaning. The ordinary meaning of that term is the significant-figure meaning. *See*, *e.g.*, *Viskase Corp. v. American Nat'l Can Co.*, 261 F.3d 1316, 1320 (Fed. Cir. 2001) (recognizing the "standard scientific convention" of significant figures); *Valeant Pharms. Int'l Inc. v. Mylan Pharms. Inc.*, 955 F.3d 25, 34 (Fed. Cir. 2020) (similar); *U.S. Philips Corp. v. Iwasaki Elec. Co.*, 505 F.3d 1371, 1377–78 (Fed. Cir. 2007) (noting that a claimed range "should not be read . . . with greater precision than the claim language warrants" based on the number of significant figures). The parties do not dispute that there is precisely one significant figure in the term "0.001%"—the "1" at the third decimal place preceded by only zeroes.

The significant-figure meaning of "0.001%" reflects its place in the entire claim phrase at issue. The phrase, in representative claim 13 of the '328 patent, is: "PVP K25 is present at a concentration of 0.001% w/w." '328 patent, col. 8, lines 62–63. The claim requires a weight ratio to be "at" a stated number, and the weight ratio is based on so many particles that it is effectively a continuous (not discrete) function. Sensibly, in this situation, Mylan does not read claim 13 as limited to a single exact point on the real-number line, but instead recognizes that the language refers to *some* interval that answers the question: How close does a result have to be to the real number 0.001% to be "at" that number? The significant-figure convention for real-world-measurement situations supplies an answer by giving a well-defined interval as the ordinary meaning, in the art, of a statement of a single number like the statement at issue here. Under this ordinary-meaning approach, the significant-figure interval meant by "0.001%" is 0.0005% to 0.0014%, based on rules of rounding and the single significant figure at the third decimal place. The district court so concluded, and Mylan has not disputed that conclusion. *AstraZeneca*, 2020 WL 4670401, at *5.

B

Mylan, accepting the need for some interval to define the "0.001%" claim term, proposes a different definition—"that precise number, with only minor variations." Mylan's Opening Br. at 20–21. In its opening brief, Mylan makes no meaningful affirmative argument for the correctness of "minor variations" as an interpretation. *Id.* at 34–45. Rather, almost its entire argument is a negative one—against the significant-figure interpretation of "0.001%"—and that argument, at every turn, relies ultimately on a single two-part point: first, the specification identifies a concentration level of "0.0005%" that the inventors tested separately from a level of "0.001%," and that AstraZeneca originally included in its claims before narrowing them during prosecution; and second, the significant-figure interval of "0.001%"

overlaps with portions of the significant-figure interval of "0.0005%" (including 0.0005% itself). *Id.* But neither on that basis nor otherwise has Mylan provided sound support for its proposed construction.

One problem with Mylan's proposed "minor variations" construction is that, without additional precision, it actually adds to the uncertainty of claim scope compared to the ordinary meaning. Such a construction works against the core purpose of claim construction, which is to *clarify* claim scope. *See*, *e.g.*, *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997) ("Claim construction is a matter of resolution of disputed meanings and technical scope, *to clarify* and when necessary to explain what the patentee covered by the claims, for use in the determination of infringement." (emphasis added)); *Arlington Indus. Inc. v. Bridgeport Fittings, Inc.*, 759 F.3d 1333, 1338 (Fed. Cir. 2014) (quoting *U.S Surgical* statement); *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co., Ltd.*, 521 F.3d 1351, 1362 (Fed. Cir. 2008) (same); *see also Avid Tech., Inc. v. Harmonic, Inc.*, 812 F.3d 1040, 1050 (Fed. Cir. 2016) (stating that "the aim of claim construction [is] to give the finder of fact an understandable interpretation of claim scope to apply to the accused systems").

Relatedly, the phrase "minor variations," without further construction to identify how much variation is too large to be "minor," effectively reinstates the "about" language that AstraZeneca used in its original claim 1 but removed in favor of the more precise "0.001%." AstraZeneca's withdrawal of its "about" language does not imply that "0.001%" was meant to have a non-interval meaning. Instead, AstraZeneca chose to express the PVP concentration with a number having a well-defined interval (the ordinary significant-figure meaning), not one having the uncertain scope of "about" or "minor variation."

For some patents, the intrinsic evidence may support displacement of the ordinary meaning (although it might

present a risk that the adopted construction is itself indefinite). But that is not so here. We "look at the ordinary meaning in the context of the written description and the prosecution history." *Medrad, Inc. v. MRI Devices Corp.,* 401 F.3d 1313, 1319 (Fed. Cir. 2005) (citations omitted). In this case, those sources simply do not show a use of "minor variations" or a comparable phrase that would accomplish the one thing Mylan insists its phrase does, namely, displace the ordinary, significant-figure meaning so as to exclude concentrations down to 0.0005% (thereby avoiding the overlap on which Mylan's argument is premised).

No such phrase is used at all in the specification, much less to imply departure from the ordinary meaning. In the prosecution history, the one phrase to which Mylan points is the examiner's mention (quoted above) of a need for AstraZeneca to show criticality by showing unexpected results of a "0.001%" concentration level compared to concentrations levels "slightly greater or less" than 0.001% PVP. Mylan's Opening Br. at 13 (quoting J.A. 16307). But nothing about that phrase implies a displacement of the ordinary significant-figure meaning. It is simply unclear if the examiner meant to *include* "0.0005%" and other tested concentration levels tested *within* the meaning of "slightly greater or less."[2] Thus, even if "slightly greater or less" is assumed to have the same meaning as "minor variations," the examiner's use of this phrase in discussing criticality does not establish the exclusion of "0.0005%," much less that "minor variations" properly replaces the ordinary significant-figure meaning of the claim phrase at issue.

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[2] The court's opinion itself seems to use "slightly" and "minor" to refer to, rather than exclude, the difference between "0.001%" and the other concentration levels whose testing is discussed in the specification. *E.g.*, Op. 8, 13, 14.

C

Mylan tries to supply more precision to the term "minor variations" by asserting that a "minor variation" here equals exactly the significant-figure interval that would exist if "0.001%" were changed to "0.0010%"—the latter having two significant figures, not one. Mylan's Opening Br. at 42 (stating that its construction is "alternatively stated as '0.0010 [%] w/w PVP'"); *see id.* at 21, 27, 33 n.7. But Mylan does not explain why "minor variations" itself has this two-significant-figure meaning. Mylan's "0.0010%" assertion amounts to an alternative construction.

On its merits, this construction should be rejected, for the simplest of claim-construction reasons. Adopting this construction requires rewriting the claim term. And that rewriting is counter to the specification and prosecution history. It is undisputed that AstraZeneca uniformly used just one significant figure when referring to PVP concentrations in its compositions, both in the specification and the prosecution history, never using more significant figures. *AstraZeneca*, 2020 WL 4670401, at *5–6. In this respect, this case is critically different from *Viskase*, in which the patentees did use an extra significant figure in the prosecution history to distinguish their invention from the prior art and this court relied on that fact in adopting its claim construction. *See* 261 F.3d at 1321–22.

Twice in its opening brief Mylan makes a passing suggestion, without development into an argument, that "the specification showed that the inventors varied PVP concentrations . . . with precision out to four decimal places." Mylan's Opening Br. at 43; *see also id.* at 27. To the extent that Mylan suggests that the use of four decimal places to state some concentration values indicates that all concentration values should be read to express a degree of precision to four decimal places, that suggestion is meritless. Most fundamentally, the specification never uses four decimal places to refer to the degree of precision of the

specified numbers, *i.e.*, the interval around the stated figure meant to be captured by that figure. The specification uses four decimal places only to refer to the *absolute concentration level*—which, if small enough, makes use of four decimal places unavoidable just to identify the level (*i.e.*, concentrations of "0.0001%" and "0.0005%" PVP). Absolute levels and degrees of precision are distinct.

Moreover, nothing in the patent suggests that the degree of precision for "0.001%" is to the fourth decimal place just because stating the absolute level for some tested concentrations—"0.0005%" and "0.0001%"—requires use of four decimal places. Indeed, Mylan has identified no basis in the patent for inferring that the degree of precision is uniform, in absolute (interval size) terms, across different absolute levels of concentration—*e.g.*, that the degree of precision at the 0.0005% concentration level must be the same as the degree of precision at the 0.001% concentration level. Of course, the ordinary significant-figure meaning is *dis*uniform in precisely that way: A single-significant-figure number written using the fourth decimal place has a significant-figure interval that is smaller in absolute terms than a single-significant-figure number written using only the third decimal place. Nothing in the patent displaces that ordinary result. And Mylan's suggestion is not aided by considering the underlying interest in suspension stability. Mylan has not argued, or pointed to any intrinsic or extrinsic evidence indicating, either that the sensitivity of suspension stability to variation is (as a scientific matter) uniform across different absolute levels of concentration or that, even if it is, any such conclusion would be clear enough to displace the ordinary meaning.

D

What remains of Mylan's argument is simply the fact that the significant-figure interval for "0.001%" overlaps with the significant-figure interval for "0.0005%"—which is the single fact to which Mylan repeatedly returns in each

section of its brief's argument about claim construction. Notably, of the various concentration levels tested and described in the specification—"0.0001%," "0.0005%," "0.001%," "0.01%," "0.03%," and "0.05%" w/w PVP—the *only* pair with overlapping significant-figure intervals is "0.0005%" and "0.001%."[3] The same is true of the prosecution history, in which, not surprisingly, AstraZeneca discussed as its invention only concentration levels reflected in the specification. So Mylan has only the single overlap to work with. But that overlap, as already explained, does not support a "minor variations" or extra-significant-digit or four-decimal-places construction. And in any event, it cannot help Mylan.

First, Mylan's argument on this score is a negative one: that the significant-figure construction is decisively wrong because (a) the specification reports that the inventors separately tested concentrations identified as "0.0005%" and "0.001%" (among other PVP amounts) and reached different conclusions about the stability of the formulations with those two levels, and (b) there is overlap between the significant-figure intervals of the two figures—respectively, 0.00045% to 0.00054%, and 0.0005% to 0.0014%. The two premises are correct, but Mylan's conclusion that overlap negates the distinction reflected in the specification is wrong.

Overlap does not imply the absence of a distinction: Two ranges—here the significant-figure intervals of two numbers—are different even if they overlap. Consider a patent in which one claim requires an amount of 3 to 7 (by

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[3] For example, the concentration "0.01%" encompasses an interval of 0.005% to 0.014%, which does not overlap with either the concentration below it, "0.001%" (significant-figure interval of 0.0005% to 0.0014%), or the concentration above it, "0.03%" (significant-figure interval of 0.025% to 0.034%).

some measure) of some component and another claim requires an amount of 1 to 4 of the same component. The two claims, despite their overlap, would still be distinct in their coverage, and—given that each covers amounts not in the other—one might be valid and the other invalid (so that, if an original application contained both claims, the applicant might withdraw one but keep the other without limiting the scope of the retained claim). Similarly, here, the significant-figure intervals of the identified figures are different, each including absolute concentration levels that are not present in the other, and so test results could differ, as the specification indicates they did. Contrary to Mylan's suggestion, the ordinary significant-figure interpretation of the two terms, "0.0005%" and "0.001%," does not erase the distinction between them just because they overlap.

Second, even if the overlap supported some limitation on the construction that defines claim scope, Mylan cannot succeed. Whether by implied disclaimer or an inference of the proper degree of precision at the "0.001%" level, the most this overlap could possibly support would be an exclusion of the small range with the one significant-figure interval for which there is overlap. Under this approach, the intrinsic evidence would limit the meaning of "0.001%" to its significant-figure interval *minus* the overlap with the significant-figure interval of "0.0005%," leaving a claim scope of 0.00055% to 0.0014% w/w PVP. But it is undisputed that Mylan's ANDA product falls within even this narrower range. Therefore, we need not decide whether this overlap-area exclusion is ultimately justified as a claim construction. Claims must be construed "only to the extent necessary to resolve the controversy." *Vivid Techs., Inc. v. American Science & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999); *see Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017).

III

For those reasons, I respectfully dissent from the majority's holding that the term "0.001%" should be construed as "that precise number, with only minor variations" or as "0.0010%." I would affirm the judgment of infringement as well as the judgment of no invalidity.