Appeal No. 2021-1729

In the 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,

Appeal from the United States District Court for the Northern District of West Virginia in Nos. 1:18-cv-00193, 1:19-cv-00203, Judge Irene M. Keeley

NON-CONFIDENTIAL COMBINED PETITION FOR PANEL REHEARING AND REHEARING EN BANC OF PLAINTIFFS-APPELLEES

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UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 2021-1729

Short Case Caption AstraZeneca AB v. Mylan Pharmaceuticals Inc.

Filing Party/Entity AstraZeneca AB; AstraZeneca Pharmaceuticals LP

Instructions: Complete each section of the form. In answering items 2 and 3, be specific as to which represented entities the answers apply; lack of specificity may result in non-compliance. **Please enter only one item per box; attach additional pages as needed and check the relevant box**. Counsel must immediately file an amended Certificate of Interest if information changes. Fed. Cir. R. 47.4(b).

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: 01/21/2022

Signature: /s/ David I. Berl

Name: David I. Berl

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	**2. Real Party in Interest.** Fed. Cir. R. 47.4(a)(2).	**3. Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☑ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
AstraZeneca AB		AstraZeneca PLC
AstraZeneca Pharmaceuticals LP		AstraZeneca PLC

☐ Additional pages attached

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

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5. Related Cases. Provide the case titles and numbers of any case known to be pending in this court or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. Do not include the originating case number(s) for this case. Fed. Cir. R. 47.4(a)(5). See also Fed. Cir. R. 47.5(b).

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6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

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☑ None/Not Applicable ☐ Additional pages attached

Confidential Material Omitted

The material omitted on page 3 indicates the concentration of PVP in Mylan's ANDA product. At Mylan's request, testimony about this information was received by the District Court under seal and the related documents were designated by Mylan as confidential under the protective order. AstraZeneca has no objection to the public disclosure of this information and has not redacted any of its own confidential information.

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STATEMENT OF COUNSEL

Based on my professional judgment, I believe the panel decision is contrary to the following precedents of this Court: *Viskase Corp. v. American Nat'l Can Co.*, 261 F.3d 1316, 1320 (Fed. Cir. 2001); *U.S. Philips Corp. v. Iwasaki Elec. Co.*, 505 F.3d 1371, 1377-78 (Fed. Cir. 2007); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (*en banc*); *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1369 (Fed. Cir. 2012); *Thorner v. Sony Comput. Entm't Am. LLC*, 669 F.3d 1362, 1365-66 (Fed. Cir. 2012).

Based on my professional judgment, I believe this appeal requires an answer to one or more precedent-setting questions of exceptional importance:

1) Whether the established, agreed-upon ordinary meaning of a numerical term in a claim may be displaced, in the absence of lexicography or disclaimer, on the basis that it may encompass more than the most preferred disclosed embodiment.

/s/ David Berl

Counsel for Plaintiffs-Appellees AstraZeneca AB and AstraZeneca Pharmaceuticals LP

POINTS OF LAW OVERLOOKED OR MISAPPREHENDED BY THE COURT

The panel majority overlooked and misapprehended, by failing to cite or apply, the controlling decisions of *Iwasaki* and *Viskase*, in holding that the ordinary meaning of a numerical claim term based on significant digits may be displaced, in the absence of lexicography or disclaimer, because it may encompass more than the most preferred embodiment.

INTRODUCTION

Numbers, like words, have ordinary meanings informed by baseline rules—here, the standard conventions of significant figures. As Judge Taranto observed in dissent, the majority abandoned the basic principles of significant figures that have long been recognized by this Court and instead "rewr[ote] the claim term," Dissent 12, from "0.001%" to "0.001**0**%." The majority's approach throws into disarray the settled expectations regarding the scope of hundreds of thousands of claims reciting numbers.

The divided panel vacated and remanded the District Court's judgment of infringement based on its revised claim construction, an issue the majority conceded was a "close call." Op.6. This case was "close" for the majority only because it disregarded entirely, and then violated flagrantly, this Court's longstanding precedent regarding the meaning of numbers in claims. *See, e.g.*, *U.S. Philips Corp. v. Iwasaki Elec. Co.*, 505 F.3d 1371, 1377-78 (Fed. Cir. 2007); *Viskase Corp. v. Am. Nat'l Can Co.*, 261 F.3d 1316, 1320 (Fed. Cir. 2001). The relevant claim term recites that "PVP K25 is present at a concentration of *0.001% w/w*," a quantity with one significant digit. That specific concentration of PVP K25 is recited repeatedly throughout the specification and prosecution history, each and every time with one significant digit. Given

the uniform intrinsic evidence, the District Court construed the term according to its plain and ordinary meaning, encompassing values that round to 0.001%: 0.0005% to 0.0014%.

In reversing, the majority construed 0.001% as "that precise number, with only minor variations, i.e., 0.00095% to 0.00104%." Op.7. Not one word of that construction comes from the intrinsic record. The patent never describes 0.001% PVP K25 as a "precise number"; never uses the phrase "minor variations"; never expresses a PVP concentration using more than one significant digit; and never references a range from 0.00095% to 0.00104%, which is, as Judge Taranto explained, "what the term would mean if it were rewritten as 0.001**0**% (adding an extra significant figure)," Dissent 2 (emphasis added), a number that appears nowhere in the intrinsic record. As the dissent recognized, a construction that "requires rewriting the claim term . . . counter to the specification and prosecution history" cannot be correct. Dissent 12.

By ignoring the ordinary, significant digit meaning of the claim term as written, the majority has extirpated, root to branch, the settled understanding in this Court's precedent, and scientific convention, that significant figures define the scope of numbers in claim terms. In contrast to the easily-applied, well-settled, and therefore seldom-litigated rules of significant digits, the

majority's approach muddies the boundaries of the hundreds of thousands of patent claims that recite numbers, frustrating the fundamental purpose of claims and upsetting the public's reliance on claim language. That issue is important and will recur every time a court must construe numbers, which are ubiquitous in patent claims. Panel rehearing or rehearing *en banc* is warranted.

BACKGROUND

AstraZeneca markets Symbicort®, a pressurized metered dose inhaler (pMDI) containing the active ingredients budesonide and formoterol, to treat respiratory diseases. Symbicort® contains several excipients, including 0.001% PVP K25, that provide stability and ensure consistent dosing. Mylan seeks to market a generic version of Symbicort® that contains the same formulation with **percentage** PVP K25.

I. AstraZeneca's Invention

At trial, AstraZeneca asserted ten claims from three patents directed to the Symbicort® formulation. Appx21-25; Appx9554 (103:4-21); Appx10070 (602:14-20). Claim 13 of U.S. Patent No. 7,759,328, representative for present purposes, recites the components of the formulation and their amounts, each with one significant digit:

> 13. A pharmaceutical composition 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.

Appx146 (8:58-64) (emphasis added). The prior art taught away from this formulation, as the District Court found, Appx39, 42-44, and the panel unanimously affirmed, Op.20-21.

The '328 patent describes the "present invention" as formulations in which "PVP is present from about 0.0005 to about 0.03%," Appx143 (1:39-45), and discloses data showing the stability of related formulations with varying concentrations of PVP K25 over that range, Appx128-142; Appx143-146 (2:64-8:15). Formulations with 0.001% gave "the best suspension stability overall," *id.* (6:30-31), but formulations with higher or lower PVP K25 concentrations within the range of 0.0001 to 0.05% also were "considered excellent." *Id.* (5:60-6:29). The patent nowhere disparages formulations with 0.0005% PVP K25, which are included repeatedly as part of the invention. Appx145 (5:5-6:31). In

contrast, in different experiments evaluating formulations with different levels of another excipient, PEG-1000, the patent disparages 0.005% PEG-1000 as "unsatisfactory." Appx146 (7:30-31). The specification contains no similar statement regarding any amount of PVP K25 within the invention, "0.0005 to about 0.03%." Appx143-146.

II. Procedural History

A. Proceedings Below

The parties disputed the meaning of "0.001%" PVP K25, and relied exclusively on intrinsic evidence. From the outset, that dispute centered on the number of significant digits that should be accorded to "0.001."

The number of significant digits conveys the rounding applicable to a number, as Mylan explained even before this litigation began, in its Paragraph IV notice letter. The first non-zero digit is significant. Appx7080. "[L]eading zeros"—zeros left of the first non-zero digit, e.g., **0.0**6—"are not significant figures regardless of whether or not a decimal point is present." *Id.* n.6. However, "[t]railing zeros"—zeros right of the decimal point and not followed by a nonzero number, e.g., 12.**00**—"are always significant when a decimal point is present." *Id.*

The number "0.001%" has one significant digit and thus encompasses values that round to that number, ranging from 0.0005% to 0.0014%. AstraZeneca consistently argued that "0.001%" should be construed as written, with one significant digit. Appx7013; Appx7382-7386. Mylan acknowledged throughout the litigation that "0.001%" encompassed *some* range of values (and never argued it was precisely that number) but countered that "0.001%" should be construed as "0.001**0**%"—i.e., 0.001% with a *second* significant digit—which would narrow the rounding range to 0.00095-0.00104%. Appx7082; Appx7027. Mylan later rebranded its proposed construction of "0.001%" as "that precise number, with only minor variations," Appx6804, but retained the same two-significant-digit rounding range.

The District Court adopted AstraZeneca's construction because it comported with the plain language, Appx63-68, while Mylan's construction "conflicts with the plain language of the claim" by "add[ing] a significant digit" without basis and thus failed to "define[] the claim with whatever specificity and precision is warranted by the language of the claim and the evidence bearing on the proper construction," Appx64 (quoting *PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1355 (Fed. Cir. 1998)).

The Court also concluded that the specification and prosecution history supported AstraZeneca's construction, not Mylan's. The specification "used '0.001%' consistently with a single significant digit." Appx65. While the specification described 0.001% PVP K25 as the preferred embodiment, the Court rejected Mylan's disclaimer argument (abandoned on appeal), because, in the specification and during prosecution, AstraZeneca never distinguished the claims through rounding "0.001%" to a second significant digit and never expressed PVP concentration with more than one significant digit. Appx66-68.

After trial, the District Court held that the patents-in-suit were not obvious and granted judgment in favor of AstraZeneca. Appx4-48.

B. Panel Decision

The panel unanimously upheld the judgment of nonobviousness, but a divided panel disagreed with the District Court's claim construction. Op.2. In what it described as a "close call," Op.6, the majority construed "'0.001%' as that precise number, with only minor variations, i.e., 0.00095% to 0.00104%," Op.7. The majority suggested that the principles of significant digits would ordinarily apply to "an abstract number on a page," but not to the numbers in these claims. *Id.* According to the majority, that was because the specification

disclosed that "formulations with 0.001% w/w PVP gave the best suspension stability overall," Op.9 (quoting Appx145 (6:30-31)), and construing "0.001%" with a single significant digit would encompass 0.0005%, the concentration of PVP K25 in another embodiment of the invention, Op.9-11. The majority also reasoned that the prosecution history supported a narrower construction, since AstraZeneca asserted only that the preferred 0.001% PVP K25 embodiment showed unexpected results. Op.12-14.

Judge Taranto dissented. Applying this Court's case law interpreting numerical claim terms that the majority never cited, let alone addressed, he would have held that the "ordinary meaning of [0.001%] is the significant-figure meaning," which has a rounding interval of 0.0005% to 0.0014%. Dissent 8. Mylan's (and the majority's) "'minor variations' construction," in contrast, "adds to the uncertainty of claim scope compared to the ordinary meaning" and thus "works against the core purpose of claim construction, which is to *clarify* claim scope." Dissent 10. Judge Taranto saw no basis to depart from the claim's acknowledged ordinary meaning. He explained that the intrinsic record never "show[ed] a use of 'minor variations' or a comparable phrase" sufficient to "displace the ordinary, significant-figure meaning" of 0.001%. Dissent 11. And the dissent would have rejected Mylan's attempt to construe

"0.001%" as "0.0010%" because it required "rewriting the claim term" without a basis in the intrinsic record. Dissent 12.

ARGUMENT

I. Panel Or En Banc Rehearing Is Warranted To Reestablish This Court's Consistent Precedent Regarding Significant Digits

A. The Majority Failed To Acknowledge That Numbers Have Ordinary Meanings Under The Principles of Significant Digits

This Court consistently has interpreted numbers in patent claims according to the "standard scientific convention" of significant digits. *Viskase*, 261 F.3d at 1320. That convention conveys to the POSA the precision "the claim language warrants"; for example, "'1' represents a less precise quantity than '1.0' and '1' may encompass values such as 1.1 that '1.0' may not." *Iwasaki*, 505 F.3d at 1377-78 (Fed. Cir. 2007) (citing *Viskase*)); *see also Valeant Pharms. Int'l Inc. v. Mylan Pharms. Inc.*, 955 F.3d 25, 34 (Fed. Cir. 2020). Those are binding precedential pronouncements, not mere suggestions that may be ignored when a case is "close." As the Dissent recognized, this court's precedent establishes that the "ordinary meaning" of a numerical claim term "is the significant-figure meaning." Dissent 8 (citing *Viskase*, *Valeant*, and *Iwasaki*). The ordinary, significant-figure meaning of numbers also has been recognized by this Court's predecessor in interpreting the prior art, *see In re*

Grose, 592 F.2d 1161, 1164-65 (C.C.P.A. 1979), as well as by sister Circuits in interpreting numbers in other contexts, *see Nat. Res. Def. Council v. E.P.A.*, 735 F.3d 873, 884 (9th Cir. 2013) (significant digits used to interpret maximum daily pesticide dose); *Nebraska v. E.P.A.*, 89 F. App'x 277, 278 (D.C. Cir. 2004) (same for maximum contaminant level). In accordance with this Court's precedent, district courts have relied on the ordinary, significant-digit meaning of numbers to interpret numbers in claim terms.[1]

This Court's consistent precedent is clear: that ordinary meaning should have governed the construction of "0.001%" here, since there was no evidence the inventors intended to opt out of the ordinary meaning of numbers, *Viskase*, 261 F.3d at 1322, and undisputedly no disclaimer of claim scope or lexicography, *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1369

[1] *See, e.g.*, *Allergan, Inc. v. Teva Pharm. USA, Inc.*, 2016 WL 7210837, at *17 (E.D. Tex. Dec. 13, 2016) (Bryson, J.) ("The patentees chose the number of significant figures to use in the claimed percentages. Those numbers would naturally be assumed to include percentages that would round up or down to [the claimed percentages]."); *Sebela Int'l Ltd. v. Taro Pharm. U.S.A.*, 2017 WL 4157380, at *4 (S.D.N.Y. Sept. 19, 2017) ("[POSA] would understand that it is 'just basic scientific knowledge' to round a value up or down based on that [rounding] range."); *Noven Pharm., Inc. v. Actavis Labs. UT, Inc.*, 2016 WL 3625541, at *5 (D. Del. July 5, 2016) (Stark, J.) (construing "15 mg/cm^2" as having "two significant figures, meaning it would be read as 15 plus or minus .5"); *Johnson Matthey Inc. v. Noven Pharm., Inc.*, 2009 WL 2208214, at *5 (E.D. Tex. July 21, 2009) (similar).

(Fed. Cir. 2012) ("Absent disclaimer or lexicography, the plain meaning of the claim controls."). AstraZeneca consistently expressed "0.001%" PVP K25 with only one significant digit throughout the specification and prosecution history, Appx65, even as the patent used additional significant digits to express other quantities with additional precision, Appx146 at 7:62-65 (reciting budesonide percentages of 62.**0**, 50.**0**, and 47.**0**).

That should have made this a straightforward case under this Court's significant-digit precedent. Both parties heavily cited this Court's decision in *Viskase*, 261 F.3d 1316, which addressed squarely the role of significant figures in construing claims. ECF 14 at 39-41; ECF 22 at 46-48; ECF 24 at 6-7, 16-17. Yet the majority ignored that precedent entirely, not citing it or even attempting the impossible feat of reconciling the panel's holding with its controlling rubric. The patentee in *Viskase* claimed polyethylenes with a "density below about 0.91 g/cm^3," 261 F.3d at 1320, but the otherwise controlling, two significant digit ordinary meaning was displaced by the prosecution history's reliance on a third significant digit—i.e., below ".91**0**"—to distinguish prior art densities of 0.910 to 0.940, *id.* at 1321-22. Because the patentee "relie[d] on the third significant figure" to distinguish prior art in prosecution, this Court held the patentee to its statements and construed the

term with a third significant digit. *Id.*; *accord Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995).

The majority could not—and did not—find that this precedent supports the construction it adopted. Unlike the patentee in *Viskase*, AstraZeneca *never* expressed "0.001%" PVP K25 with an additional significant digit, either in the specification or prosecution history. *See* Dissent 12 ("[T]his case is critically different from *Viskase*[.]"). The majority points to occasions during the prosecution history when AstraZeneca sought claims to other concentrations of PVP K25, Op.12-13, and established that 0.001% PVP K25 specifically achieved unexpected results, Op.14, but those numbers were likewise expressed with one significant digit. At no point did the majority suggest that these statements constituted a disclaimer of claim scope.

Instead of applying or attempting to distinguish this Court's significant-digit precedent, the majority relegated the rules of significant digits to interpreting "an abstract number on a page," Op.7, rather than a number in a claim term. The majority's *sub silentio* abrogation of this Court's significant-digits precedent replaces those well-accepted, predictable rules with an analysis that requires rewriting unambiguous claim terms to a level of precision found nowhere in the intrinsic evidence in order to limit them to the

preferred embodiment in the specification. That unwarranted and unprecedented approach will sow uncertainty for hundreds of thousands of claims that recite numerical limitations, as the majority's own analysis reflects.

B. The Majority Contravened Precedent By Replacing The Controlling Rules Of Significant Digits With Discredited Claim Construction Principles

The meaning of a number is governed by the "standard scientific convention" of significant digits, *Viskase*, 261 F.3d at 1320; *see Iwasaki*, 505 F.3d at 1377, except where the patent or prosecution history clearly demonstrates a different meaning, such as in cases of lexicography or disclaimer, *Viskase*, 261 F.3d at 1321-22; *see Phillips*, 415 F.3d at 1316; *Toshiba*, 681 F.3d at 1369 (citing *Thorner v. Sony Comput. Entm't Am. LLC*, 669 F.3d 1362, 1366 (Fed. Cir. 2012)). The majority declined to address this precedent, Op.7, and substituted an analysis that was legally erroneous in multiple respects.

The majority rewrote the claims. "[C]ourts may not redraft claims," even if the result would be "nonsensical." *Chef Am., Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371, 1374 (Fed. Cir. 2004). Yet that its precisely what the majority did here.

No part of the majority's construction of "0.001%"—"that precise number, with only minor variations, i.e., 0.00095% to 0.00104%," Op.7—has intrinsic support. The phrases "precise number" and "minor variations" never appear in the specification or prosecution history. Unsurprisingly, Mylan advanced "no meaningful affirmative argument" in support of its proposed rewriting of the claim language, Dissent 9, and the majority improperly assumed that it should be adopted automatically, without an assessment of its propriety, upon a finding that AstraZeneca's construction was imperfect.

But more importantly, as Judge Taranto explained, Mylan's construction confoundingly "adds to the uncertainty of claim scope compared to the ordinary meaning," contrary to the basic purpose of claim construction "to *clarify* claim scope." Dissent 10. At best, "that precise number, with only minor variations" is empty verbiage. The business end of the majority's construction is the range "0.00095% to 0.00104%," which is unambiguously what would be conveyed by the number "0.001**0**%," Dissent 2—that is, 0.001% expressed with an extra significant digit, contrary to the rules of significant digits firmly ensconced in this Court's claim construction jurisprudence.

In other words, significant digits ultimately control the majority's construction, despite the majority's effort to refute their applicability. Mylan

conceded as much. ECF 14 at 42. The problem with construing "0.001%" as "0.0010%" is simple: it "requires rewriting the claim term," Dissent 12, contrary to the intrinsic record, and in the admitted absence of any lexicography or disclaimer. ECF 14 at 44 (Mylan conceding that its construction "does not depend on disavowal or disclaimer"). The number "0.0010%" appears nowhere in the patent or file history. By redrafting the claim term with an additional significant digit, the majority commits precisely the error identified by this Court in *Iwasaki*: expressing "a quantity with greater precision" than the claims warrant. 505 F.3d at 1377-78 ("incorrect" to construe "10^{-x}" as "$1.\underline{0} \times 10^{-x}$" instead of "$1 \times 10^{-x}$" (emphasis added)).

The majority limited the claims to a redefined version of the preferred embodiment. In lieu of a cognizable basis to depart from the ordinary meaning of "0.001%," the majority seized on the specification's comparison of multiple embodiments of the invention, including formulations with 0.001% and 0.0005% PVP K25. Op. 9-11. But that is simply no basis for excluding from the claims 0.0005%, which remains an embodiment different from 0.001% PVP K25 under that term's ordinary meaning. *See Continental Circuits LLC v. Intel Corp.*, 915 F.3d 788, 798 (Fed. Cir. 2019) ("comparing and contrasting" embodiments insufficient to depart from claim's ordinary

meaning). As the dissent explained, some overlap in the rounding ranges of 0.001% and 0.0005% still leaves both numbers with a unique meaning. "Two ranges—here the significant-figure intervals of two numbers [0.001% and 0.0005%]—are different even if they overlap." Dissent 14 (only portion of the significant-digit range of 0.001% overlaps with the 0.00045% to 0.00054% significant-digit range of 0.0005%).

Thus, the majority's redrafting of the unambiguous claim term as written to another unambiguous, but unwritten, term relies not on any established principle of claim construction, but rather is based on an impetus to limit the claims to the preferred embodiment, to the exclusion of other inventive embodiments encompassed within the term's ordinary meaning. But that impetus has no place in this Court's claim construction jurisprudence, especially where, as here, precedent dictates the limited circumstances that permit displacement of the significant-digit meaning. *See Viskase,* 261 F.3d at 1320; *see also Phillips*, 415 F.3d at 1323; *Linear Tech. Corp. v. Int'l Trade Comm'n*, 566 F.3d 1049, 1057-58 (Fed. Cir. 2009). The patent describes 0.001% PVP K25 as the preferred embodiment that provided the "best suspension stability overall," Op.8-9, but the patent does not (as Mylan concedes, ECF 14 at 44) disclaim other concentrations of PVP K25, including 0.0005%. Rather,

it describes the "present invention" as formulations in which "PVP is present from about 0.0005 to about 0.03%," Appx143 (1:39-45), and characterizes multiple formulations with concentrations between 0.0001 and 0.05% as "excellent." Appx145 (5:60-6:29). That 0.001% PVP K25 "is more stable" than 0.0005% cannot justify uprooting this Court's clear significant figures pronouncements to limit the claims to a version of the preferred embodiment *redefined at a level of precision entirely absent from the intrinsic record.* Op. 10. *See Viskase*, 261 F.3d at 1320; *Iwasaki*, 505 F.3d at 1377-78.

Contrary to the majority's holding, there is simply nothing "acontextual" (Op.12) or improper about a claim term encompassing multiple inventive embodiments. And even were the majority correct that the 0.0005% embodiment fell outside the scope of the claims, the proper construction, as the dissent recognized, 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." Dissent 15. The majority ignored that construction, which unlike the construction it adopted, has support in its (mis)interpretation of the specification.

Contrary to the basic principles of mathematics, and this Court's significant figure precedents, the majority finds significance in the "fourth

decimal place[s]" implied in its 0.0010% construction, and the percent variation of its rounding range. Op.15. But neither consideration finds any support in the intrinsic evidence, and both contravene this Court's repeated precedents that significant digits, not the number of decimal points or rounding range variation, dictate the precision accorded to numerical claim terms. As the dissent explained, "[t]he 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." Dissent 13. The majority did not respond to this basic, irrefutable mathematical proposition. And the patent never suggests that its numbers have a degree of precision corresponding to the number of decimal places. *Id.* That same principle also dispenses with the majority's percent-variation approach, mentioned only in passing, Op.15, as it also improperly tethers the precision of a quantity to its absolute level without evidentiary support. Regardless, the majority never suggests that this intrinsic evidence justifies departure from the controlling precedents of *Viskase* and *Iwasaki*, which it ignores altogether.

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The majority's approach leads to confusion. The decision provides no guidance regarding when the public may rely on what this Court consistently (before this case) indicated was the ordinary, significant-digit meaning of claims with numbers. The majority's reasoning leaves uncertain the interpretation of multiple numbers even in the asserted '328 patent, where, "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%.'" Dissent 14. Does that mean that "0.05%" also carries precision to the "fourth decimal place," Op.12, 15, thereby engrafting *two* significant digits ("0.05**00**%"), or would the ordinary meaning apply because its rounding-range with one significant digit (0.045-0.054%) does not overlap with the preferred embodiment (or other tested embodiments), Op.9?

The majority's approach injects uncertainty, where none existed, into hundreds of thousands of patents. It requires redrafting claim terms arbitrarily to distinguish between multiple embodiments that fall within the claim term as written and are described as part of the invention. That approach traduces this Court's precedent, which the panel neither acknowledged nor applied, that the ordinary and predictable rules of

significant digits govern absent clear intrinsic evidence to the contrary. The panel or *en banc* Court should rehear this case to reestablish its longstanding precedent setting forth the ordinary meaning of numbers.

CONCLUSION

Panel rehearing or rehearing *en banc* should be granted.

JANUARY 21, 2022

Respectfully submitted,

/s/ David Berl

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CERTIFICATE OF SERVICE

I certify that today, January 21, 2022, I electronically filed the foregoing Brief for Plaintiffs-Appellees with the Clerk of the Court for the U.S. Court of Appeals for the Federal Circuit using the appellate CM/ECF system. Counsel of record for all parties will be served by the appellate CM/ECF system.

/s/ David Berl
DAVID BERL

JANUARY 21, 2022

Attorney for Plaintiffs-Appellees

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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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:

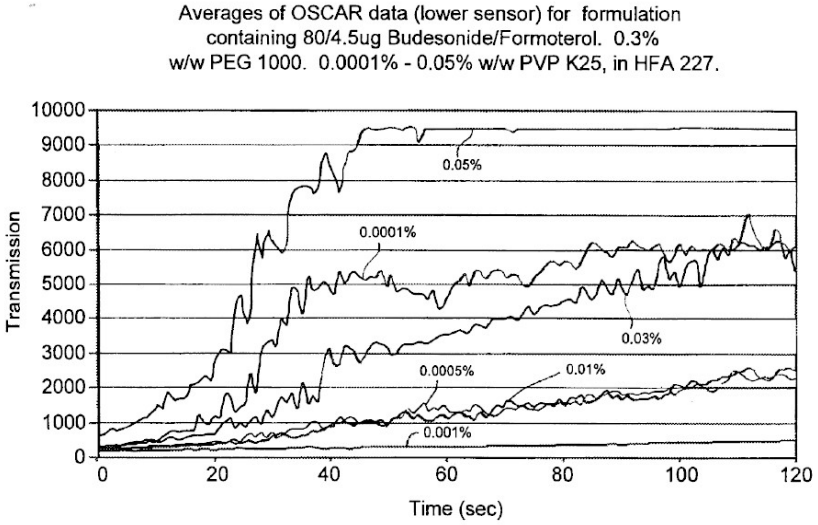

FIG. 3

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:

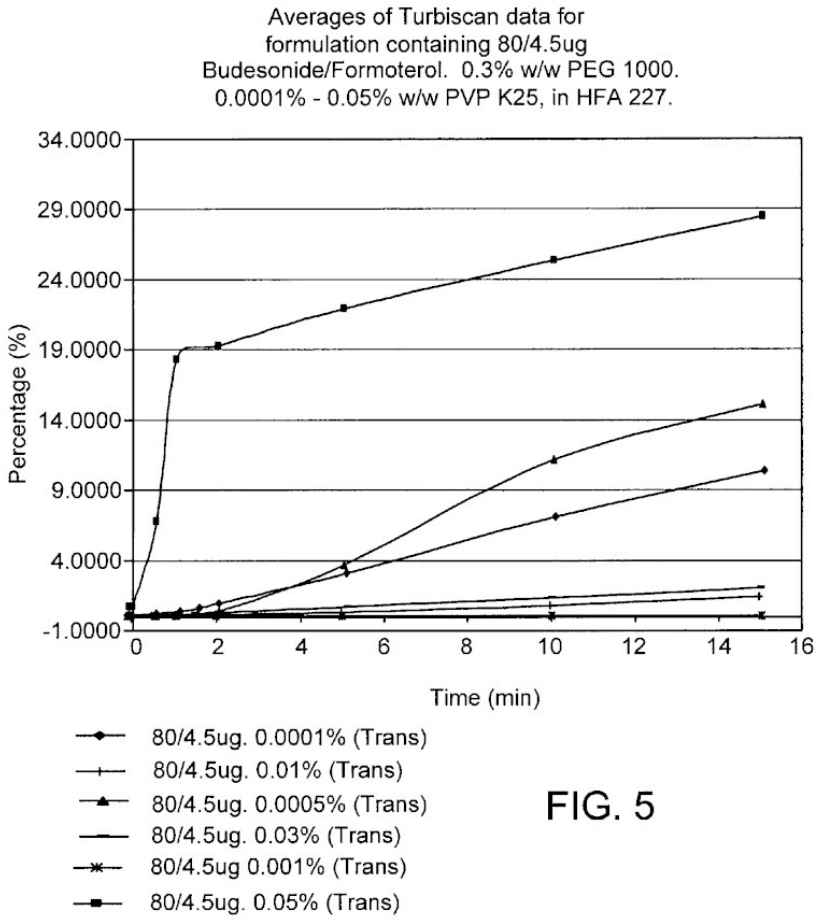

FIG. 5

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. AztraZeneca'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.

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1. This brief complies with the type-volume limitation of Fed. R. App. P. 32(b)(2)(A). This brief contains 3900 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b).

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