No. 2021-1729

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.

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

BRIEF FOR *AMICUS CURIAE* PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA (PhRMA) SUPPORTING PANEL REHEARING, REHEARING EN BANC, AND REVERSAL

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February 4, 2022

CERTIFICATE OF INTEREST

Counsel for Amicus Curiae Pharmaceutical Research and Manufacturers of America certifies as follows:

1. Represented Entities. Fed. Cir. R. 47.4(a)(1). Provide the full names of all entities represented by undersigned counsel in this case.

Pharmaceutical Research and Manufacturers of America ("PhRMA")

2. Real Party in Interest. Fed. Cir. R. 47.4(a)(2). 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.

3. Parent Corporations and Stockholders. Fed. Cir. R. 47.4(a)(3). 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.

PhRMA has no parent corporation and no publicly held corporation owns 10% or more of its stock. However, its membership includes companies that have issued stock or debt securities to the public. A list of PhRMA's members is available at: www.phrma.org/About.

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).

None.

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).

None.

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).

None.

Dated: February 4, 2022

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INTEREST OF *AMICUS CURIAE*

Pharmaceutical Research and Manufacturers of America (PhRMA) is a voluntary, nonprofit association of leading innovative biopharmaceutical companies.[1]

PhRMA's members are the primary source of the many new drugs and biologics introduced each year, which play a key role in extending longevity and improving the quality of human life. These medical advances require enormous investments—both to account for the significant failure rate associated with innovative research and to comply with legal requirements to demonstrate the safety and efficacy of new medicines. Since 2000, PhRMA members have invested more than $1 trillion in the search for new treatments, including $91.1 billion in 2020 alone.

The protections of patent law provide incentives for companies like PhRMA's members to take on the huge risks and astronomical costs of biopharmaceutical development. For those incentives to work effectively, there must be stability and predictability in patent law, including clear and fixed rules

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[1] PhRMA certifies that no party or party's counsel or person other than PhRMA's members and counsel authored in whole or in part or contributed money that was intended to fund the preparation or submission of this brief. AstraZeneca Pharmaceuticals LP is a member of PhRMA but did not participate in the preparation of this brief. A complete list of PhRMA members is available at http://www.phrma.org/About.

governing claim construction. PhRMA's members rely on having an effective understanding of their patent claims for purposes of making investment decisions and defending and asserting their rights. As discussed below, the panel majority's decision creates significant uncertainty by departing from the "significant figure" convention, a well-established scientific practice for expressing and interpreting numbers. PhRMA has a strong interest in maintaining the clarity and stability achieved by that convention.

SUMMARY OF THE ARGUMENT

The plain meaning of numbers in patents and scientific publications has traditionally been guided by application of the "significant figure" convention, under which the number of significant digits in a value indicates the degree of precision intended. The panel majority's decision deviates from this convention and complicates the analysis of what constitutes the "ordinary meaning" of numbers.

Relying on the specification and prosecution history, the panel majority effectively rewrote the claimed concentration "0.001%" as if it said "0.0010%," with an additional significant digit. But the evidence that the panel cited was too weak to overcome the plain meaning of the claim term under the significant figure convention. The convention provides a widely accepted rule for reciting numbers,

and every deviation from it undermines its usefulness. Accordingly, courts should not depart from the convention absent exceptional circumstances.

Moreover, courts must be mindful that the significant figure convention is a tool for interpreting not just the plain meaning of claim language but also numbers in the specification and prosecution history. The panel majority lost sight of this principle. Notably, the statements from the specification and prosecution history on which the panel majority relied continued to recite 0.001% with only one significant digit, not the further degree of precision imputed by the panel majority. When read in light of the significant figure convention, the specification and prosecution history reinforce the ordinary meaning of the claims.

By effectively sidelining the significant figure convention, the panel majority's decision sows confusion over how courts should interpret numbers in patent claims. This will encourage more litigation and increase unpredictability, frustrating incentives to innovate. For these reasons, rehearing is warranted.

ARGUMENT

I. THE SIGNIFICANT FIGURE CONVENTION IS A WELL-ESTABLISHED STANDARD

The significant figure convention—widely accepted and applied by the scientific community—is the standard practice for expressing and ascertaining a number's precision. For example, when a value is reported as 1.48, it is

understood that the first two digits are known with confidence and the last digit is an approximation. *See generally* Rao, *Numerical Analysis* 2-3 (2006) (explaining the general rule of significant digits). The recited number 1.48 would thus be understood to include values that round to 1.48 (*i.e.*, 1.475 to 1.484). In contrast, the number 1.480, recited with an additional digit, would convey greater precision and be understood to include a narrower range of values (*i.e.*, 1.4795 to 1.4804).

All non-zero digits (and zeros between non-zero digits) are considered significant. Rao, *supra*, at 2-3. For example, 8009 has four significant digits. In numbers with decimal points, leading zeros before the first non-zero digit are not significant, while trailing zeros after the last non-zero digit are significant. For example, 0.00809 has three significant digits, while 0.008090 has four significant digits.

The scientific community has repeatedly impressed the importance of using the significant figure convention to standardize the meaning of numbers in scientific research. Laboratories insist on the adoption of this standard for the measurement, calculation, and synthesis of analytical data. *See, e.g.*, Scarlata, et al., *Rounding and Significant Figures*, Laboratory Analytical Procedure 1 (2005) ("It is the responsibility of each analyst recording analytical data to comply with each of these rules for significant figures and rounding."). Academics urge the application of the well-accepted standard for reporting numbers with significant

figures. *See, e.g.*, Dunn, *Measurement, Data Analysis, and Sensor Fundamentals for Engineering and Science* 550 (2011) ("It goes without saying that the proper use of significant figures is an essential element in the presentation of both experimental and calculated results and their uncertainties.").[2] And educators at all levels instill the fundamentals of these bedrock principles in students nationwide.[3]

Indeed, this Court has already recognized the importance of the significant figure convention and of not ascribing to a number a greater degree of precision than specified. *See U.S. Philips Corp. v. Iwasaki Elec. Co.*, 505 F.3d 1371, 1377-1378 (Fed. Cir. 2007) (warning that numbers in claim language "should not be read … with greater precision than the claim language warrants" and recognizing that "in some scientific contexts, '1' represents a less precise quantity than '1.0,' and '1' may encompass values such as 1.1 that '1.0' may not[.]"); *Viskase Corp. v. American Nat'l Can Co*., 261 F.3d 1316, 1320 (Fed. Cir. 2001) (acknowledging

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[2] *See also* Stephenson, *Calculations for Molecular Biology and Biotechnology: A Guide to Mathematics in the Laboratory* 1 (2004) ("The numerals of a measurement representing actual limits of precision are referred to as significant digits."); Gierlinski, *Understanding Statistical Error: A Primer for Biologists* 6.4 (2016) ("Significant figures (or digits) are those that carry meaningful information. In most cases, [the remaining digits] are by-products of calculations carried out to higher precision than that of the original data. … You should never, ever quote them in a publication.").

[3] *See, e.g*., Busser, *Significance and Accuracy in Measurements*, 18 BioScience 1125-1128 (1968) (explaining that high school students are educated on the convention of rounding off and significant figures).

the convention of rounding off based on a number's significant figures "is a standard scientific convention"); *see also Valeant Pharms. Int'l Inc. v. Mylan Pharms. Inc.*, 955 F.3d 25, 34 (Fed. Cir. 2020) (applying the significant figure convention to claimed pH ranges).

The importance of heeding the precision with which a number is recited cannot be overstated. The convention is grounded in sound scientific principles, and its widespread acceptance promotes clarity by establishing a common understanding of reported values. The ubiquity of the significant figure convention distinguishes it from other evidence sometimes offered to prove plain meaning. It is not like a dictionary definition or an example of a term's use in prior art—both of which can be clouded by the presentation of conflicting evidence. The significant figure convention is *the* standard scientific practice for expressing numbers. It thus should be given substantial weight in claim construction and should not be cast aside without compelling reasons.

II. THE SIGNIFICANT FIGURE CONVENTION SHOULD INFORM EVERY STEP OF CLAIM CONSTRUCTION

The panel majority's ruling in this case gave insufficient weight to the significant figure convention. As discussed below, this deviation from the standard will have consequences far beyond this case.

The panel majority's decision focused on construing the term "0.001%." Op. 4. The parties, the majority opinion, and Judge Taranto's dissent all agreed that the plain meaning of 0.001% is its meaning under the significant figure convention, which would "encompass a range from 0.0005% to 0.0014%." Op. 7; Dissent 8 ("It is undisputed that the term '0.001%' here … has an ordinary meaning" which "is the significant-figure meaning."). The panel majority acknowledged that "[t]his is a standard scientific convention." Op. 7.

But after stating that it was "a close call," the panel majority construed 0.001% as "that precise number, with only minor variations, i.e., 0.00095% to 0.00104%." Op. 6-7. In other words, the panel majority effectively read the claim as if it recited 0.0010%, permitting only the variation that would have been allowed if the claim had been written differently.

The panel majority based this departure from the plain and ordinary meaning on its reading of the specification and prosecution history, stating that it would not adopt an "acontextual construction." Op. 7. But the panel majority failed to factor the significant figure convention into its understanding of the specification and prosecution history.

For example, the panel majority stressed AstraZeneca's narrowing of its claims during prosecution from "about 0.0005 to about 0.05 %" to "0.001%." Op. 12. But, in relying on that evidence, the panel majority misconstrued where the

narrowing stopped. The specific number AstraZeneca used was 0.001%. Had AstraZeneca intended to narrow its claims further, it would have added another significant digit to say 0.0010%. *See Viskase*, 261 F.3d 1316 (interpreting the claimed number with an additional significant digit was appropriate because the number recited in the specification included additional digits). Though some claims were narrowed over time, AstraZeneca gave no indication when it settled on 0.001% that it was abandoning the plain meaning of 0.001%.

Similarly, when the Examiner said that AstraZeneca needed to test "slightly more and less than 0.001%," Op. 13 (emphasis omitted), there was no indication that the Examiner was referring to an unusually narrow band around 0.001% rather than the standard significant figure understanding of that term. The specification compares the stability of a 0.001% formulation to various other concentrations, not just the 0.0005% concentration that would produce a slight overlap with 0.001% when both values are interpreted under the significant figure convention. *See* Dissent 11.[4]

By limiting application of the significant figure convention, the panel majority created a conflict between the claim language and the specification and

[4] Moreover, as Judge Taranto explains, even if there were a problem with this slight overlap between the 0.001% and 0.0005% concentrations, it could be avoided with a slightly narrower construction without otherwise abandoning the significant figure convention. *See* Dissent 15.

prosecution history where none exists. Had it considered the discussion of all numerical values in the specification and prosecution history using the significant figure convention, it would have been clear that the intrinsic evidence supports a reading of 0.001% as written—*i.e.*, its plain meaning with one significant digit. Courts should not ignore a patentee's decision to use a particular number of significant figures, and there is no compelling need here to disturb the plain meaning of 0.001% when it can be read consistently with other intrinsic evidence.

III. REHEARING IS WARRANTED TO RESTORE CONSISTENT APPLICATION OF THE SIGNIFICANT FIGURE CONVENTION

If left undisturbed, the panel majority's decision will create confusion regarding the scope of patents, which will have a long-lasting effect on the incentives afforded by the patent system and the advancement of scientific progress. By departing from the significant figure convention without stronger evidence of intent to do so, the panel majority's decision casts doubt on how much weight will be given to this standard practice. This is not merely a case-specific issue. The importance of having an established standard for communicating the precision of numbers is self-evident: It reduces transaction costs and clarifies the scope of patent rights. Every departure from the significant figure convention diminishes its value as a common means of expressing numbers across all patents.

The effect of the uncertainty created could be far reaching. Thousands of patents, and particularly biopharmaceutical patents, include scope-determining numbers in the form of weights, concentrations, pH levels, etc. In the absence of clear principles for construing numbers, claim construction will become more burdensome and unpredictable. Patent owners will have to fear the increased likelihood of a court construing claimed numbers or ranges contrary to their intent. Likewise, potential competitors and the public will have less guidance to determine the meaning and scope of a claim.

Uncertainty regarding claim scope diminishes the incentive to invest and innovate because innovators weighing investment decisions and parties to commercial transactions cannot be certain that clearly expressed claims will be given their proper scope. *See, e.g.*, Beighley, *The Court of Appeals for the Federal Circuit: Has it Fulfilled Congressional Expectations?*, 21 Fordham Intell. Prop. Media & Ent. L.J. 671, 736 (2011) ("Uncertainty in the patent system prevents inventors from counting on patents …."); Newman, *The Federal Circuit—A Reminiscence*, 14 Geo. Mason U. L. Rev. 513, 515 (1992) ("the degree of legal certainty, as to patentability and enforceability, is a significant factor in innovation decisions").

This lack of certainty is particularly concerning in the biopharmaceutical industry where research and development requires massive investment and is

marked by a high failure rate. *See* Schelhorn, *The Promise and Peril of Industry-Specific Patent Law*, 22 Va. J.L. & Tech. 161, 164-165 & n.10 (2019) ("the reliance on patent protection is of particular importance in the pharmaceutical industry" given the "massive investments in new drugs, a lengthy development process and a high risk of failure"); *see also* DiMasi, *Innovation in the Pharmaceutical Industry*, 47 J. Health Econ. 20, 31 (2016).

The Supreme Court has noted that "courts must be cautious before adopting changes that disrupt the settled expectations of the inventing community." *Festo Corp. v. Shoketsu*, 535 U.S. 722, 739-740 (2002); *see also Immersion Corp. v. HTC Corp.*, 826 F.3d 1357, 1364 (Fed. Cir. 2016) ("Investment-backed expectations and reliance interests in patent law are often strong."). Countless inventions have been disclosed and patented in reliance on the use of well-established principles like the significant figure convention. Weakening of the convention threatens to upend those expectations.

Beyond patent owners, the public at large also has an interest in the consistent application of claim construction principles so that it has sufficient notice of the boundaries of patent claims to avoid infringement. Uncertain claim scope also diminishes "the so-called 'negative incentive' to 'design around'" a patent. *See State Indus. Inc. v. A.O. Smith Corp.*, 751 F.2d 1226, 1236 (Fed. Cir. 1985). The easier it is for a potential competitor to convince a court to depart from an

established standard, the more incentive there is to invest in litigation rather than innovation. This will negatively impact judicial economy and divert resources from more productive endeavors.

This Court was created to bring more uniformity to the interpretation and enforcement of patents. *See* S. Rep. No. 97-275, at 2 (1981), *reprinted in* 1982 U.S.C.C.A.N. 11, 12; *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 390 (1996) ("Congress created the Court of Appeals for the Federal Circuit as an exclusive appellate court for patent cases, observing that increased uniformity would 'strengthen the United States patent system in such a way as to foster technological growth and industrial innovation.'" (citations omitted)). Given this special charge, the Court should take this opportunity to correct, or at least clarify, the law concerning the weight of the significant figure convention in determining the plain and ordinary meaning of numbers in patent claims.

CONCLUSION

The Court should grant AstraZeneca's petition for rehearing.

Respectfully submitted,

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February 4, 2022

CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATIONS

The foregoing filing complies with the relevant type-volume limitation of the Federal Rules of Appellate Procedure and Federal Circuit Rules because:

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