No. 20-1074

IN THE

United States Court of Appeals

FOR THE FEDERAL CIRCUIT

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AND AMGEN USA, INC.,

Plaintiffs-Appellants,

v.

SANOFI, AVENTISUB LLC, FKA AVENTIS PHARMACEUTICALS INC., REGENERON PHARMACEUTICALS INC., AND SANOFI-AVENTIS U.S. LLC,

Defendants-Appellees.

On Appeal from the United States District Court
for the District of Delaware, in No. 1:14-cv-01317-RGA

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UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 20-1074

Short Case Caption Amgen Inc., et al. v. Sanofi, et al.

Filing Party/Entity Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA, Inc.

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: 04/14/2021

Signature: /s/ Jeffrey A. Lamken

Name: Jeffrey A. Lamken

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
Amgen Inc.	None	None
Amgen Manufacturing, Limited	None	Amgen Inc.
Amgen USA, Inc.	None	Amgen Inc.

☐ 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).

☐ None/Not Applicable ☑ Additional pages attached

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/Not Applicable ☐ Additional pages attached

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/Not Applicable ☐ Additional pages attached

CERTIFICATE OF INTEREST

Appellants Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA, Inc. (collectively "Amgen") state that the following partners or associates have appeared on their behalf before the district court or are expected to appear in this Court:

From **Young Conaway Stargatt & Taylor LLP**: Melanie K. Sharp, James L. Higgins, and Michelle M. Ovanesian.[1]

From **McDermott Will & Emery LLP**: William G. Gaede, III, Sarah C. Columbia, K. Nicole Clouse, Mandy H. Kim, Bhanu K. Sadasivan, David L. Larson, Rebecca Harker Duttry, Eric W. Hagen, Terry W. Ahearn, Shane G. Smith, Michael V. O'Shaughnessy, Esther E. Lin, and Evan Boetticher.[2]

From **Schertler & Onorato, LLP**: Christopher B. Mead.

From **Cravath, Swaine & Moore LLP**: Keith R. Hummel, David N. Greenwald, Lauren A. Moskowitz, Andrei Harasymiak, Geoffrey G. Hu, Sharonmoyee Goswami, and Amal Elbakhar.

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[1] Michelle M. Ovanesian no longer practices with Young Conaway Stargatt & Taylor LLP and is not expected to enter an appearance on behalf of Amgen in this appeal.

[2] Eric W. Hagen, Terry W. Ahearn, Shane G. Smith, Michael V. O'Shaughnessy, Esther E. Lin, and Evan Boetticher no longer practice with McDermott Will & Emery LLP and are not expected to enter appearances on behalf of Amgen in this appeal.

From **Quinn Emanuel Urquhart & Sullivan, LLP**: Lauren N. Martin and Megan Y. Yung.[3]

From **King & Spalding LLP**: Daryl L. Joseffer and Adam M. Conrad.[4]

From **Amgen, Inc.**: Stuart L. Watt, Wendy A. Whiteford, Erica S. Olson, Steven D. Tang, Emily C. Johnson, Dennis J. Smith, and Joshua Mack.[5]

From **MoloLamken LLP**: Jeffrey A. Lamken, Michael G. Pattillo, Jr., Sarah J. Newman, and Sara E. Margolis.[6]

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[3] Megan Y. Yung no longer practices with Quinn Emanuel Urquhart & Sullivan, LLP, and is not expected to enter an appearance on behalf of Amgen in this appeal.

[4] Daryl L. Joseffer and Adam M. Conrad no longer practice with King & Spalding LLP and are not expected to enter appearances on behalf of Amgen in this appeal.

[5] Joshua Mack is no longer employed by Amgen, Inc., and is not expected to enter an appearance on behalf of Amgen in this appeal.

[6] In the prior appeal in this case (No. 17-1480), Christopher R. Healy, Merritt E. McAlister, and Joshua N. Mitchell from King & Spalding LLP appeared before this Court on behalf of Amgen. Those attorneys are not expected to enter appearances on behalf of Amgen in this appeal.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

CASES

CONSTITUTIONAL PROVISIONS & STATUTES

OTHER AUTHORITIES

STATEMENT OF COUNSEL CONCERNING REHEARING EN BANC

Overturning the jury's enablement determination, the panel decision in this case announced a new and heightened standard for genus claims with functional limitations—a test that, according to the panel, "pose[s] ***high hurdles***" and "***raises the bar*** for enablement." Op. 11, 12 (emphasis added). Rather than examine whether the specification fails to enable particular embodiments, the new test evaluates the "'time and effort'" required to make and test every candidate so as "***to reach the full scope of claimed embodiments***." Op. 14 (emphasis added). Deeming enablement "a question of law . . . review[ed] without deference," Op. 6, the panel repeatedly resolved key disputed factual issues contrary to the jury's implicit findings.

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

1. Whether the panel's new enablement test for genus claims with functional limitations, which has no basis in § 112's text, conflicts with Supreme Court decisions, including *Minerals Separation, Ltd. v. Hyde*, 242 U.S. 261 (1916); *Wood v. Underhill*, 46 U.S. (5 How.) 1 (1846); and *Mowry v. Whitney*, 81 U.S. (14 Wall.) 620 (1872), and decisions of this Court and its predecessor, including *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234 (Fed. Cir. 2003), and *In re Angstadt*, 537 F.2d 498 (C.C.P.A. 1976).

2. Whether enablement is a question of fact, as the Supreme Court has held, *see Battin v. Taggert*, 58 U.S. (17 How.) 74 (1854); *Wood v. Underhill*, 46 U.S. (5 How.) 1 (1846), or a question of law, as this Court holds, Op. 6.

/s/ Jeffrey A. Lamken
Jeffrey A. Lamken

Counsel for Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA Inc.

INTRODUCTION

The panel decision announces a new test that does not merely "raise[ ] the bar for enablement" for genus claims. Op. 12. It threatens to invalidate an entire category of such claims.

This Court had long required that specifications enable POSAs "to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). That requirement focused on whether it would require undue experimentation to practice particular embodiments. Under that standard, invalidity required concrete proof of an embodiment within the claims that was not enabled.

The panel's decision announces a different test for genus claims with functional limitations—common in biotechnology and pharmaceutical patents—one that "pose[s] ***high hurdles*** in fulfilling the enablement requirement." Op. 11 (emphasis added). Under it, enablement is evaluated by the "'time and effort'" required "***to reach the full scope*** of ***claimed embodiments***," Op. 14 (emphasis added)—*i.e.*, the effort to make and test each "candidate" so as to identify every embodiment that meets the claimed function. The effect is to invalidate virtually any genus claim with functional limitations, even if the disclosure makes generating and testing any single embodiment routine. The decision is the culmination of recent cases that

"dramatically" change enablement law, to the point where now "it is nearly impossible to have a valid genus claim." D. Karshtedt, M. Lemley & S. Seymore, *The Death of the Genus Claim*, at 1 (Aug. 5, 2020) ("*KLS*"), https://ssrn.com/abstract=3668014.

This case illustrates the profound impact. Confronted by the rich disclosures of Amgen's patents, Sanofi-Regeneron failed to identify ***even one embodiment*** of the claimed genus that could not be made quickly and easily. Two separate juries found Amgen's claims enabled. The panel nonetheless held the claims' "full scope" not enabled because, in its view, finding the embodiments "outside the scope of the disclosed examples" would require "generat[ing] and then screen[ing] each" of "millions of candidate[]" antibodies for the claimed function. Op. 13-14. It did not matter that the patents' roadmap, which employs standard antibody-science techniques like immunized transgenic mice, generates claimed antibodies ***every time***. Amgen.Br.32-34. It did not matter that generating and testing the hypothesized "millions" of further candidates—almost all minor variants produced by making tiny changes to ***disclosed*** embodiments—was routine. Amgen.Br.42-46, 60-61. Nor did it matter that not one of the hypothesized "millions" was shown to fail when tested, and that testing would thus exclude only rare hypothetical failures. Amgen.Br.56-60. Far from sending skilled artisans hunting for a needle in a haystack of unproven

candidates, the specification showed exactly how to make the claimed antibodies, every time.

The panel's test—the "'time and effort'" "to reach the full scope of claimed embodiments"—departs from statutory text: Section 112 asks whether POSAs can "make and use" the "invention," not how much work is required to identify all embodiments. It conflicts with Supreme Court precedent, which upholds enablement even when there are "infinite[]" embodiments, and POSAs must perform "preliminary tests" on each to discover the "precise treatment" required. *Minerals Separation, Ltd. v. Hyde*, 242 U.S. 261, 270-71 (1916). And it "misunderstand[s] . . . the purposes the law is supposed to serve." *KLS*, *supra*, at 4. The panel's test renders breakthrough inventions with the broadest application least likely to receive protection. To satisfy it, innovators must divert scarce resources from discovering life-saving innovations to rote generation of redundant embodiments to foreclose speculation about whether other hypothetical "candidates" might have the claimed functionality. Op. 9-10, 14. It threatens investment in "biotech, chemical, and pharmaceutical" innovation, which "make[s] heavy use of genus claims" for which functional characterization is part of the lexicon of the science. *KLS*, *supra*, at 2-3.

The decision conflicts with Supreme Court precedent in a second respect. This Court holds that enablement "is a question of law . . . review[ed] without deference." Op. 6. The Supreme Court has held the opposite. This Court's contrary

view invites panels to disregard a jury's factual determinations in favor of the panel's own view. For that reason, too, en banc review is warranted.

BACKGROUND

I. AMGEN'S INVENTION

This appeal concerns Amgen's U.S. Patent Nos. 8,829,165 and 8,859,741, which describe and claim a breakthrough invention: antibodies that dramatically lower LDL cholesterol levels. The claims cover a genus of antibodies that bind to a tiny, specified region—encompassing 15 amino acids out of 700—on a protein called "PCSK9." The antibodies thereby block PCSK9 from binding to and interfering with the body's LDL receptors, which remove LDL cholesterol from blood. *See* Amgen.Br.5-9.

Amgen's patents are a "rich handbook" with a "wealth of information." Appx3910(763:1-12). They characterize 26 specific embodiments representing—as the jury found and the district court upheld—the diversity of the claimed genus. *See* Appx51-116(Figs. 2A-3JJJ); Appx240(85:9-12, 85:35-43); Appx9-11. The patents provide a "roadmap" that teaches POSAs to use traditional techniques, like immunizing transgenic mice, to obtain the other antibodies within the claims. Amgen.Br.13-16. The patents also explain how to predictably create functionally identical "variants" of the working antibody examples through "conservative" substitution. Appx221(48:21-33); Appx3902(733:12-22); Amgen.Br.16-17.

II. PROCEDURAL HISTORY

Two juries have found Amgen's patents valid. After the first jury rejected Sanofi-Regeneron's written-description and enablement challenges, the district court denied JMOL. Appx2061-2065; Appx2885. On appeal, this Court ordered a new trial on written description and enablement, citing an erroneous jury instruction and evidentiary ruling excluding post-priority-date antibodies. *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1375-82 (Fed. Cir. 2017).

On remand, a second jury found for Amgen, despite Sanofi-Regeneron's presentation of four post-priority-date antibodies that, according to Sanofi-Regeneron, defeat written description and enablement. The district court upheld the jury's verdict on written description, Appx7-11, but granted JMOL on enablement, Appx11-25.

A panel of this Court affirmed. Enablement, the panel announced, "is a question of law that we review without deference," although evaluating "'undue experimentation'" involves "'weighing'" various "'factual considerations.'" Op. 6-7. Under § 112, the panel explained, "a patent's specification must 'enable'" POSAs "'to make and use' the patented invention." Op. 6. This Court's precedents require that the specification enable "the full scope of the claimed compounds" without "undue experimentation." Op. 9. The panel agreed that the full-scope requirement

traditionally required parties challenging enablement to provide "concrete identification of at least some embodiment or embodiments asserted not to be enabled." Op. 10-11 (quotation marks omitted). Despite that precedent, the panel did not identify a single concrete, non-enabled embodiment.

The panel, however, invoked an alternative test—purportedly from *Wyeth & Cordis Corp. v. Abbott Laboratories*, 720 F.3d 1380 (Fed. Cir. 2013), *Enzo Life Sciences, Inc. v. Roche Molecular Systems, Inc.*, 928 F.3d 1340 (Fed. Cir. 2019), and *Idenix Pharmaceuticals LLC v. Gilead Sciences Inc.*, 941 F.3d 1149 (Fed. Cir. 2019)—for genus claims with functional elements. According to the panel, such claims confront "high hurdles in fulfilling the enablement requirement," and "'undue experimentation can include'" the effort to "'identify[], from among the many concretely identified compounds that meet the structural requirements, the compounds that satisfy the functional requirement.'" Op. 11.

Under that test, the panel held, "practic[ing] the full scope of [Amgen's] claims" would require "undue experimentation." Op. 14. Repeatedly resolving disputed factual issues contrary to Amgen's evidence and the jury's implied findings, the panel found that "the claims encompass[] millions of candidates"; that the antibody arts are "unpredictable"; and that the patents lack "adequate guidance" beyond "the [specification's] working examples." Op. 12-14. "[N]o reasonable jury could conclude," the panel held, "that anything but 'substantial time and effort' would be

required ***to reach the full scope*** of ***claimed embodiments***." Op. 14 (emphasis added).

ARGUMENT

I. THE NEW ENABLEMENT TEST IMPOSED HERE WARRANTS EN BANC RECONSIDERATION

Despite the Supreme Court's repeated admonishment that this Court should not "impose limitations on the Patent Act that are inconsistent with the Act's text," *Bilski v. Kappos*, 561 U.S. 593, 612 (2010), the panel's decision does just that. Departing from § 112's text, the decision announces a separate enablement standard that "raises the bar" for genus claims, Op. 12—a test that does not ask whether the specification enables POSAs to "make and use" the invention, but asks how much "'time and effort'" is required "***to reach the full scope*** of claimed embodiments," Op. 14 (emphasis added). That test defies Supreme Court precedent. And it defies the purpose of patent law, invalidating breakthrough inventions based on scope alone, and demanding disclosures that contribute nothing to progress of the useful arts.

A. The Panel's Enablement Standard Defies Text and Precedent

Section 112 requires a "description of the invention" sufficient "to enable" POSAs "to make and use the same." 35 U.S.C. § 112(a). The specification must teach POSAs "how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech*, 108 F.3d at 1365.

The full-scope requirement long focused on whether undue experimentation would be required to practice particular embodiments. Challengers had to provide "concrete identification of at least some embodiment" within the claim that was not enabled. *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 (Fed. Cir. 2020). For example, the "full scope" of a claim covering alloys with "up to about 10%" silicon was not enabled where the specification did not teach alloys with more than 0.5% silicon. *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1239, 1244-45 (Fed. Cir. 2003). The "full scope" requirement was not met for claims covering mechanical and electronic sensors where the specification did not enable electronic sensors. *Auto. Techs. Int'l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274, 1285 (Fed. Cir. 2007).

A different full-scope test has recently emerged for genus claims "that state certain structural requirements and also require performance of some function." *McRO*, 959 F.3d at 1100 n.2. That test examines whether "undue experimentation" is required "in identifying, from among the many concretely identified compounds that meet the structural requirements, the compounds that satisfy the functional requirement." *Id.* That test initially ferreted out specifications that left POSAs "searching for a needle in a haystack," randomly screening thousands upon thousands of compounds in the hopes of finding ***any*** that satisfy functional limitations. *Idenix*, 941 F.3d at 1162. It thus addressed disclosures that were merely research

plans to test a sea of "candidates" to find any embodiments. *Cf. Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984) (claims not enabled only when "number of inoperative combinations becomes significant").

The decision in this case, however, fundamentally changes the test. It directs courts to examine the "'time and effort'" required "to reach the full scope of claimed embodiments." Op. 14 (emphasis added). It thus does not examine the effort required to find ***any*** embodiment, but the effort to find ***every*** embodiment. Indeed, unlike in *Idenix*, *Wyeth*, and *Enzo*, the panel here identified no evidence of a high failure rate that would leave POSAs searching for a needle in a haystack to practice the invention. There was ample proof that the patents' roadmap generates claimed antibodies ***every time***. Appx3896-3897(709:2-711:11). Amgen's expert testified that the roadmap produces the full scope of claimed antibodies. Appx3908(757:12-14); Appx3909(762:14-20). The evidence showed that "conservative substitution"—the technique the panel invoked to arrive at the posited "millions of candidates"—reliably produced working variants. Amgen.Br.43-49. Sanofi-Regeneron introduced ***no*** evidence that the technique ***ever*** failed to produce working variants here, much less that it did so with any frequency. Amgen.Br.56-60; p. 17 n.1 *infra*. The jury is presumed to have found that dispositive. *See Arctic Cat Inc. v. Bombardier Recreational Prods. Inc.*, 876 F.3d 1350, 1358, 1364 (Fed. Cir. 2017).

While the panel declined to characterize "the effort required to ***exhaust*** a genus" as "dispositive," Op. 13, that vague disclaimer does not mitigate the new test's impact. Whether the "'time and effort'" "to reach the full scope of claimed embodiments" means making and testing every "candidate" to identify every unexemplified embodiment, or virtually every embodiment, or some unspecified large portion, the result is the same: Patents with functional limitations now lack enablement, no matter how routine it is to make any embodiment, simply because the genus is large. The ability to make numerous minor structural variants becomes fatal, even when using reliable techniques taught in the patent and prior art. Amgen.Br.43-49. If testing is necessary to achieve 100% certainty—to exclude only hypothetically possible non-working outliers—the claim is not enabled. *Id.*

That defies statutory text and precedent. Because § 112 requires only that the specification enable POSAs to "make and use" the claimed invention, enablement asks whether the specification "guide[s] those skilled in the art to" the "successful application" of "the invention." *Minerals Separation*, 242 U.S. at 271; *see Universal Oil Prods. Co. v. Globe Oil & Refin. Co.*, 322 U.S. 471, 484 (1944) (specification must teach POSAs "to practice the invention"). That is "'a standard of reasonableness.'" *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). For 200 years following the first Patent Act, no court suggested that enablement depends on the "'time and effort'" necessary to make and test every conceivable member of a genus "to reach

the full scope of claimed embodiments." Op. 14. Section 112 nowhere provides a separate or heightened "full scope of claimed embodiments" test for claims with functional limitations.

The Supreme Court's *Minerals Separation* decision forecloses that test. The patent there claimed "'improvements in the process for the concentration'" of a genus of ores by separating out non-metals. 242 U.S. at 263. There were "infinite[]" varieties of ore, and POSAs would have to conduct "preliminary tests" to identify the "precise treatment" for each. *Id*. at 270-71. That patent thus would fail the panel's test: The "'time and effort'" necessary for POSAs "to reach the full scope" of those infinite variations—testing for each ore—would be enormous. Op. 14. But the Supreme Court upheld the claim, explaining that "it is obviously impossible to specify in a patent the precise treatment" for each variation. 242 U.S. at 271. It was enough that POSAs could successfully apply the process to a particular ore. *Id.*; *see also Wood v. Underhill*, 46 U.S. (5 How.) 1, 5-6 (1846); *Mowry v. Whitney*, 81 U.S. (14 Wall.) 620, 644-45 (1872).

The panel's test also defies this Court's precedents. The specification need not "describe how to make and use every possible variant of the claimed invention." *AK Steel*, 344 F.3d at 1244; *see In re Angstadt*, 537 F.2d 498, 503 (C.C.P.A. 1976). As Judge Bryson explained, enablement should not turn on the experimentation

"required for one artisan to synthesize all members of the genus." *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629, 661 (E.D. Tex. 2017) (Bryson, J.), *aff'd*, 739 F. App'x 643 (Fed. Cir. 2018) (mem.). "Such a rule," he explained, "would invalidate all broad claims for lack of enablement." *Id.*

B. The New Standard Threatens Innovation

The panel's departure from traditional requirements threatens patents for breakthrough inventions—like Amgen's here—without serving any patent-law policy. The patent bargain requires patentees to disclose their inventions "in sufficient detail to enable one skilled in the art to practice the invention once the period of the monopoly has expired." *Universal Oil*, 322 U.S. at 484. Patentees satisfy their side of the bargain if the specification "guide[s] those skilled in the art to" the invention's "successful application." *Minerals Separation*, 242 U.S. at 271. The new test for genus claims, however, "abandon[s] a practical focus on whether others could make use of the claimed invention in favor of a fruitless search for the exact boundaries of that invention." *KLS*, *supra*, at 4. The Court has never identified any valid purpose for demanding that POSAs be able to make, identify, and test ***all*** (or even most) potential embodiments with minimal "'time and effort.'" Op. 14. "The validity of a claim should not depend on whether others can identify and test ***all*** of them." *KLS*, *supra*, at 4.

The panel's new, distinct test threatens devastating consequences for biotech and pharmaceutical patents. "The central feature of patent law in the chemical, biotechnology, and pharmaceutical industries is the genus claim." *KLS*, *supra*, at 1. Because "'testing'" may be necessary to be 100% certain compounds function as intended, Op. 12-13, courts can now deem the effort to synthesize and screen "candidate[s]" for the genus to be undue experimentation based on the potential number of candidates alone, even where POSAs would consider such work "'routine.'" *Idenix*, 941 F.3d at 1163.

The panel's rule reduces a formerly practical inquiry into a numbers game—one that is practically "impossible" to satisfy for any "genus of any nontrivial size," *KLS*, *supra*, at 4, as commentator after commentator now recognizes, *see, e.g.*, Adam Houldsworth, *The CAFC's* Amgen v Sanofi *Decision Spells Trouble for Broad Functional Patent Claims*, iam (Feb. 16, 2021) (panel decision "entrenche[s] an approach to enablement . . . that make[s] it difficult to uphold broad genus claims in the life sciences"), https://bit.ly/3tf5k4Q; Dennis Crouch, *Functional Claim "Raises the Bar for Enablement,"* PatentlyO (Feb. 16, 2021), https://bit.ly/3tf5skQ; Dani Kass, *Biologics Face Tougher Patent Scrutiny After Amgen Ruling*, Law360 (Feb. 18, 2021), https://bit.ly/2Q5fvKM; Ed Silverman, *A U.S. Court Ruling May Force Biologics Makers To Review Patent Protections*, Stat+ (Feb. 25, 2021), https://bit.ly/3uzmzhD.

The consequences are sweeping. Any patent with a functional element, in any field, is now at risk of invalidation if the claim covers more than the exemplified embodiments. Such attacks are emerging already. *See*, *e.g.*, *Ex Parte Beall*, No. 2020-001026, 2021 WL 1208966, at *3 (P.T.A.B. Mar. 26, 2021) (invoking panel's decision to hold that patent for glass with dispersed crystalline and glass phases fails to enable "full scope" because of experimentation required "to synthesize" full range of "glass-based material covered by the recited structure" and "determine whether they meet the functional requirements").

The patent system exists to "promote the Progress" of the "useful Arts." U.S. Const. Art. I, § 8, cl. 8. The panel's rule defies that purpose. Breakthroughs often lie in identifying the mechanism for producing a desired effect and making functional embodiments. But the mechanism may have the same effect for a genus of structurally similar embodiments. If patentees could claim only disclosed embodiments, copyists could "avoid infringement" by making a "minor change" while "still exploiting the benefits of [the] invention." *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 966 (Fed. Cir. 2002). Genus claims are essential to ensuring that inventions with broad application receive commensurately broad protection. To obtain such claims, inventors now must draft prolix disclosures, with superfluous exemplary embodiments, to foreclose speculation about distinct, undisclosed embodiments. That adds nothing useful to public knowledge. And it consumes scarce

scientific resources better devoted to promoting progress. Multiplied across ***every*** genus patent, the misallocation of resources is staggering.

II. THIS COURT SHOULD RECONSIDER WHETHER ENABLEMENT IS A QUESTION OF LAW

A. This Court's Rule Conflicts with Supreme Court Precedent and Longstanding Circuit Decisions

For over 150 years, the Supreme Court has recognized that enablement is "a question of fact to be determined by the jury." *Wood*, 46 U.S. (5 How.) at 4. It is "the right of the jury to determine, from the facts in the case, whether" a patent "enable[s] any person skilled in the [art] to make the [claimed invention]." *Battin v. Taggert*, 58 U.S. (17 How.) 74, 85 (1854). Before this Court's creation, most circuits agreed that "[w]hether the description . . . is clear enough to enable a person of ordinary skill to construct or make [the invention] is a question for the jury." *A.B. Dick Co. v. Barnett*, 288 F. 799, 800 (2d Cir. 1923); *see Tights, Inc. v. Stanley*, 441 F.2d 336, 343 (4th Cir. 1971); *Rsch. Prods. Co. v. Tretolite Co.*, 106 F.2d 530, 533 (9th Cir. 1939).

This Court adopted the opposite view in a single sentence, in a footnote, declaring that "[e]nablement under [§ 112] is a question of law." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960 n.6 (Fed. Cir. 1983). *Raytheon* did not mention the contrary authority. Yet it remains the governing rule. Op. 6. It also makes no sense. Enablement and written description are derived from the same sentence of § 112.

But this Court deems one a legal question and the other factual. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1366 (Fed. Cir. 2010) (en banc) (Rader, J., dissenting-in-part and concurring-in-part). The lines the Court draws between fact and legal questions are "inexplicable." *Anascape, Ltd. v. Nintendo of Am., Inc.*, 601 F.3d 1333, 1342 (Fed. Cir. 2010) (Gajarsa, J., concurring).

B. This Case Illustrates the Importance of This Recurring Issue

Whether enablement is a fact question or legal conclusion has profound effects. Here, the panel asserted that "[f]acts control and . . . so does the standard of review," Op. 9—and then cast aside the jury's implied findings under the guise of deciding a legal question. Ordinarily, courts may overturn a verdict only where "no reasonable jury could have failed to conclude that" the party challenging enablement had established its case "by clear and convincing evidence." *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1353 (Fed. Cir. 2003). All evidence must be viewed "in the light most favorable to the jury's verdict, drawing reasonable factual inferences and resolving issues of credibility in favor of the verdict." *Bio-Tech. Gen. Corp. v. Genentech, Inc.*, 267 F.3d 1325, 1329 (Fed. Cir. 2001).

Here, the "factual considerations" derived from *Wands*, Op. 6-7, were submitted to the jury, which found that Sanofi-Regeneron failed to prove, by clear-and-

convincing evidence, that practicing Amgen's claims would require undue experimentation, Appx2906-7; Appx3631. Liberated by this Court's view that enablement "is a question of law" reviewed "without deference," Op. 6, the panel repeatedly resolved disputes over the *Wands* factors contrary to the jury's implicit findings. The panel declared, for example, that Amgen's "claims were indisputably broad," "encompass[ing] millions of candidates." Op. 12, 14. But the panel recognized that "[t]he parties dispute[d]" the size of the claimed genus, Op. 12, and the jury heard evidence that the claims "are very narrow," Appx3883 (658:1-5), encompassing at most 400 distinct antibodies, Amgen.Br.21.[1] The panel determined that "this invention is in an unpredictable field of science," Op. 12, but the district court recognized "conflicting testimony as to the predictability of the art," Appx17-18. Significantly, the panel concluded that the patents do not provide "adequate guidance" on making embodiments beyond "the [specification's] working examples." Op. 13. But experts testified that skilled artisans following the patents' roadmap "would be certain to

[1] The panel derived "millions," Op. 14, by positing that conservative substitution—a prior-art technique that ***starts*** with disclosed working antibodies and involves tiny changes designed to preserve function, Amgen.Br.42-49—hypothetically could yield that many variants. But the panel displaced the jury's implicit and factually supported determination that such small changes do not produce meaningfully distinct antibodies from the original, *id.*, imposing its own unsupported view that they do. The panel deemed each such variant a "candidate" that must be tested, Op. 14, when Sanofi-Regeneron offered ***no evidence*** that conservative substitution here ***ever*** yielded a variant that did not function like the original working antibody, Amgen.Br.46-49.

make all of the claim's antibodies." Appx3909(762:10-20); *see* Amgen.Br.32-34; Appx3918-3919(798:25-799:5). While the panel suggested that the patents do not enable antibodies that bind more than 9 sweet-spot residues, Op. 12 & n.1, Amgen's experts testified that the patents' roadmap produced the post-priority-date antibodies Sanofi-Regeneron identified, which bind 12-15 residues—and the jury agreed, *see* Appx3903(736:1-7); Appx3908-3909(757:12-760:21); Amgen.Reply.Br.27.

The panel should not have so reweighed the evidence. Clarifying that enablement is a fact question will restore the Court to its proper appellate role.

CONCLUSION

Rehearing is warranted.

April 14, 2021

Respectfully submitted,

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ADDENDUM

United States Court of Appeals for the Federal Circuit

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AMGEN USA, INC.,
Plaintiffs-Appellants

v.

SANOFI, AVENTISUB LLC, FKA AVENTIS PHARMACEUTICALS INC., REGENERON PHARMACEUTICALS INC., SANOFI-AVENTIS U.S. LLC,
Defendants-Appellees

2020-1074

Appeal from the United States District Court for the District of Delaware in Nos. 1:14-cv-01317-RGA, 1:14-cv-01349-RGA, 1:14-cv-01393-RGA, 1:14-cv-01414-RGA, Judge Richard G. Andrews.

Decided: February 11, 2021

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Before PROST, *Chief Judge*, LOURIE and HUGHES, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Amgen Inc., Amgen Manufacturing, Ltd., and Amgen USA, Inc. (collectively, "Amgen") appeal from a decision of the United States District Court for the District of Delaware granting Judgment as a Matter of Law ("JMOL") of lack of enablement of claims 19 and 29 of U.S. Patent 8,829,165 (the "'165 patent") and claim 7 of U.S. Patent 8,859,741 (the "'741 patent"). *See Amgen Inc. v. Sanofi*, No. CV 14-1317-RGA, 2019 WL 4058927, at *1–2, *13 (D. Del. Aug. 28, 2019) ("*Decision*"). For the reasons set forth below, we affirm.

BACKGROUND

Elevated low-density lipoprotein ("LDL") cholesterol is linked to heart disease. LDL receptors remove LDL cholesterol from the blood stream, thus regulating the amount of circulating LDL cholesterol. The proprotein convertase subtilisin/kexin type 9 ("PCSK9") enzyme regulates LDL receptor degradation. PCSK9 binds to LDL receptors and mediates their degradation, thus decreasing the number of LDL receptors on a cell's surface. Antibodies may bind to and block PCSK9, allowing LDL receptors to continue regulating the amount of circulating LDL cholesterol.

Amgen owns the '165 and '741 patents, which describe antibodies that purportedly bind to the PCSK9 protein and lower LDL levels by blocking PCSK9 from binding to LDL receptors. The '165 and '741 patents share a common written description. *See* Appellants' Br. 10 n.2. The specification discloses amino acid sequences for twenty-six antibodies, including the antibody (designated as "21B12")

with the generic name of evolocumab, marketed by Amgen as Repatha®. *See* '165 patent col. 85 ll. 1–43; Appellants' Br. 11 n.3. As shown for example in Figure 20A of the '165 patent, the specification discloses three-dimensional structures for the antibodies designated 21B12 and 31H4 and shows where those antibodies bind to PCSK9. The '165 and '741 patents claim antibodies that bind to one or more of fifteen amino acids (*i.e.*, "residues") of the PCSK9 protein and block PCSK9 from binding to LDL receptors.

The relevant '165 patent claims are:

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.
>
> 19. The isolated monoclonal antibody of claim 1 wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3.
>
> 29. A pharmaceutical composition comprising an isolated monoclonal antibody, wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO: 3 and blocks the binding of PCSK9 to LDLR by at least 80%.

'165 patent col. 427 l. 47–col. 430 l. 23.

The relevant '741 patent claims are:

> 1. An isolated monoclonal antibody that binds to PCSK9, wherein the isolated monoclonal antibody binds an epitope on PCSK9 comprising at least one of residues 237 or 238 of SEQ ID NO: 3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.
>
> 2. The isolated monoclonal antibody of claim 1, wherein the isolated monoclonal antibody is a neutralizing antibody.
>
> 7. The isolated monoclonal antibody of claim 2, wherein the epitope is a functional epitope.

'741 patent col. 427 ll. 36–57. The claimed antibodies are defined by their function: binding to a combinations of sites (residues) on the PCSK9 protein, in a range from one residue to all of them; and blocking the PCSK9/LDLR interaction.

This is the second time that these patents have been on appeal in our court. Amgen filed suit against Sanofi, Aventisub LLC, Regeneron Pharmaceuticals Inc., and Sanofi-Aventis U.S. LLC (collectively, "Sanofi") on October 17, 2014, alleging infringement of multiple U.S. patents, including the '165 and '741 patents. *Decision* at *1. Amgen and Sanofi stipulated to infringement of selected claims (including '165 patent claims 19 and 29 and '741 patent claim 7) and tried issues of validity to a jury in March 2016. *Id.* During the trial, the district court granted JMOL of nonobviousness and of no willful infringement. *Id.* At the close of the trial, the jury determined that the patents were not shown to be invalid for lack of enablement and written description. *Id.*

Sanofi appealed to this court. Relevant to the current appeal, we held that the district court erred in its evidentiary rulings and jury instructions regarding Sanofi's defenses that the patents lack written description and enablement, and we remanded for a new trial on those

issues. *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1381–82 (Fed. Cir. 2017). We also vacated the permanent injunction. *Id.*

On remand, the parties tried the issues of written description and enablement to the jury. The jury again found that Sanofi failed to prove that the asserted claims were invalid for lack of written description and enablement. Sanofi moved for JMOL and, in the alternative, for a new trial. *Decision* at *1; J.A. 895. The district court granted Sanofi's Motion for JMOL for lack of enablement and denied the motion for lack of written description. *See Decision* at *17; J.A. 35. The court also conditionally denied Sanofi's motion for a new trial. *Id.* Amgen timely appealed, and we have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1). *See* J.A. 909–10.

DISCUSSION

Whether a claim satisfies the enablement requirement of 35 U.S.C. § 112 is a question of law that we review without deference, although the determination may be based on underlying factual findings, which we review for clear error. *See Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014). The statutory basis for the enablement requirement is found in Section 112 of the patent statute, which provides in relevant part that a patent's specification must "enable any person skilled in the art . . . to make and use" the patented invention. 35 U.S.C. § 112(a). The purpose of the enablement requirement is to ensure that the public is told how to carry out the invention, *i.e.*, to make and use it. We have held that such disclosure must be "at least commensurate with the scope of the claims." *Crown Operations Int'l v. Solutia Inc.*, 289 F.3d at 1367, 1378–79 (Fed. Cir. 2002) (citing *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999)).

"To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence

that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" *Alcon Research*, 745 F.3d at 1188 (quoting *In re Wands*, 858 F.2d 731, 736–37 (Fed. Cir. 1988)). "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *Wands*, 858 F.2d at 737. Those factual considerations, which have come to be known as the "*Wands* factors," are:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id.

As we have stated elsewhere, "[a]fter the challenger has put forward evidence that some experimentation is needed to practice the patented claim, the factors set forth in *Wands* then provide the factual considerations that a court may consider when determining whether the amount of that experimentation is either 'undue' or sufficiently routine such that an ordinarily skilled artisan would reasonably be expected to carry it out." *Alcon Research*, 745 F.3d at 1188 (quoting *Wands*, 858 F.2d at 737). Although a specification does not need to "describe how to make and use every possible variant of the claimed invention, when a range is claimed, there must be reasonable enablement of the scope of the range." *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 (Fed. Cir. 2020) (citing *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003)) (internal citations omitted).

On appeal, Amgen asks us to reverse the district court's decision holding '165 patent claims 19 and 29 and '741 patent claim 7 invalid for lack of enablement. Amgen

contends that, under a proper analysis of the *Wands* factors, the claims at issue were enabled because no undue experimentation is required to obtain antibodies fully within the scope of the claims. Amgen points to expert testimony purportedly showing that a person of skill in the art can make all antibodies within the scope of the claims by following a roadmap using anchor antibodies and well-known screening techniques as described in the specification or by making conservative amino acid substitutions in the twenty-six examples. Amgen argues that the court erred by focusing on the effort required to discover and make every embodiment of the claims, *see* Appellants' Br. 32 (citing *Decision* at *7), while failing to recognize that Sanofi could not identify any antibody that cannot be made by following the specification's teachings. *See* Reply Br. 4–5; *see also McRO*, 959 F.3d at 1104 ("[A] usual requirement [is] that the challenger identify specifics that are or may be within the claim but are not enabled."). Amgen contends that the embodiments in the patent are structurally representative for the purpose of fulfilling the written description requirement, and such evidence is sufficient to indicate a structure/function correlation establishing enablement. *See* Reply Br. 23–24.

Sanofi responds that the district court properly concluded based on the *Wands* factors that the claims are not enabled because they require undue experimentation. As support for its position, Sanofi contends that there are millions of antibody candidates within the scope of the claims, the disclosures do not provide sufficient guidance, antibody generation is unpredictable, and practicing the full scope of the claims requires substantial trial and error. *See* Appellees' Br. 17–18, 56. According to Sanofi, the functionally defined claims cover a vast scope. *See id.* at 34–41. Sanofi argues that Amgen focused on "the number of antibodies actually known to satisfy the claims, when this court's precedents require examining the number of candidates

that must be made and tested to determine whether they satisfy the claimed function." *Id.* at 18.

We begin by considering the *Wands* case itself, which has become the "go to" precedent for guidance on enablement, and which also involved claims relating to antibody technology. The broadest claim in *Wands* "involve[d] immunoassay methods for the detection of hepatitis B surface antigen by using high-affinity monoclonal antibodies of the IgM isotype." *Wands*, 858 F.2d at 733. The U.S. Patent and Trademark Office Board of Patent Appeals and Interferences had found that undue experimentation would be required for one skilled in the art to make the claimed antibodies used in the methods because "production of high-affinity IgM anti-HBsAg antibodies [was] unpredictable and unreliable." *Id.* at 735. We found, reviewing the facts, that the disclosure adequately taught using hybridoma technology to produce the needed claimed antibodies. *See id.* at 734. We stated that "no evidence was presented by either party on how many hybridomas would be viewed by those in the art as requiring undue experimentation to screen," *id.* at 740, and we accordingly held that the specification fully enabled the claimed invention, *see id.* at 736.

Importantly, although *Wands* gave birth to its eponymous factors, *Wands* did not proclaim that all broad claims to antibodies are necessarily enabled. Facts control and, in this court, so does the standard of review. In considering the *Wands* factors, the district court compared the present case to other cases in which we found lack of enablement due to the undue experimentation required to make and use the full scope of the claimed compounds that require a particular structure and functionality. For example, in *Wyeth & Cordis Corp. v. Abbott Laboratories*, we held that claims covering methods of preventing restenosis with compounds having certain functionality requirements were invalid for lack of enablement. *See* 720 F.3d 1380, 1385–86 (Fed. Cir. 2013). Of particular significance, we held that due to the large number of possible candidates

within the scope of the claims and the specification's corresponding lack of structural guidance, it would have required undue experimentation to synthesize and screen each candidate to determine which compounds in the claimed class exhibited the claimed functionality. *Id.*

Similarly, in *Enzo Life Sciences, Inc. v. Roche Molecular Systems, Inc.*, we found that the claims were similar to those at issue in *Wyeth* in that they required both a particular structure and functionality, and we held that the specification failed to teach one of skill in the art whether the many embodiments of the broad claims would exhibit that required functionality. *See* 928 F.3d 1340, 1345–48 (Fed. Cir. 2019). And, in *Idenix Pharmaceuticals LLC v. Gilead Sciences Inc.*, we affirmed the district court's determination that the claims had both structural and functional limitations, and that undue experimentation would have been required to synthesize and screen the billions of possible compounds because, given a lack of guidance across that full scope, finding functional compounds would be akin to finding a "needle in a haystack." 941 F.3d 1149, 1160–63, 1165 (Fed. Cir. 2019); *see Idenix Pharms. LLC v. Gilead Scis., Inc.*, 2018 WL 922125 (D. Del. Feb. 16, 2018). The district court found that *Wyeth*, *Enzo*, and *Idenix* all support its conclusion that the asserted claims lack enablement. *See Decision* at *9–13.

What emerges from our case law is that the enablement inquiry for claims that include functional requirements can be particularly focused on the breadth of those requirements, especially where predictability and guidance fall short. In particular, it is important to consider the quantity of experimentation that would be required to make and use, not only the limited number of embodiments that the patent discloses, but also the full scope of the claim. As we recently explained:

> [C]onducting the *Wands* analysis has routinely involved concrete identification of at least some

> embodiment or embodiments asserted not to be enabled—including what particular products or processes are or may be within the claim, so that breadth is shown concretely and not just as an abstract possibility, and how much experimentation a skilled artisan would have to undertake to make and use those products or processes.

McRO, 959 F.3d at 1100. We then elaborated in a footnote that:

> In cases involving claims that state certain structural requirements and also require performance of some function (e.g., efficacy for a certain purpose), we have explained that undue experimentation can include undue experimentation in identifying, from among the many concretely identified compounds that meet the structural requirements, the compounds that satisfy the functional requirement.

Id. at 1100 n.2 (citations omitted).

That reasoning applies here. While functional claim limitations are not necessarily precluded in claims that meet the enablement requirement, such limitations pose high hurdles in fulfilling the enablement requirement for claims with broad functional language. *See, e.g.*, *Wyeth*, 720 F.3d at 1384 (finding that practicing the full scope of the claims would require excessive experimentation); *Enzo*, 928 F.3d at 1345 (finding that the specification failed to teach whether the many embodiments would be both hybridizable and detectable upon hybridization); *Idenix*, 941 F.3d at 1155–56 (finding that the broad functional limitation of having efficacy against hepatitis C virus increased the number of nucleoside candidates that would need to be screened).

Each appealed claim in this case is a composition claim defined, not by structure, but by meeting functional limitations. We agree with the district court's finding that the

specification here did not enable preparation of the full scope of these double-function claims without undue experimentation. *See Decision* at *13. The binding limitation is itself enough here to require undue experimentation.

Turning to the specific *Wands* factors, we agree with the district court that the scope of the claims is broad. While in and of itself this does not close the analysis, the district court properly considered that these claims were indisputably broad. The parties dispute the exact number of embodiments falling within the claims. However, we are not concerned simply with the number of embodiments but also with their *functional* breadth. Regardless of the exact number of embodiments, it is clear that the claims are far broader in functional diversity than the disclosed examples.[1] If the genus is analogized to a plot of land, the disclosed species and guidance "only abide in a corner of the genus." *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1299–300 (Fed. Cir. 2014). Further, the use of broad functional claim limitations raises the bar for enablement, a bar that the district court found was not met.

We also agree with the district court that this invention is in an unpredictable field of science with respect to satisfying the full scope of the functional limitations. One of Amgen's expert witnesses admitted that translating an antibody's amino acid "sequence into a known three-dimensional structure is still not possible." J.A. 3910; *see also Decision* at *9. Another of Amgen's experts conceded that "substitutions in the amino acid sequence of an antibody can affect the antibody's function, and testing would be

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[1] For example, there are three claimed residues to which not one disclosed example binds. *See* J.A. 4283; Appellees' Br. 52. And although the claims include antibodies that bind up to sixteen residues, none of Amgen's examples binds more than nine. *See id.*

required to ensure that a substitution does not alter the binding and blocking functions." J.A. 3891; *see also Decision* at *9. And while some need for testing by itself might not indicate a lack of enablement, we note here the conspicuous absence of nonconclusory evidence that the full scope of the broad claims can predictably be generated by the described methods. Instead, we have evidence only that a small subset of examples of antibodies can predictably be generated.

Although the specification provides some guidance, including data regarding certain embodiments, we agree with the district court that "[a]fter considering the disclosed roadmap in light of the unpredictability of the art, any reasonable factfinder would conclude that the patent does not provide significant guidance or direction to a person of ordinary skill in the art for the full scope of the claims." *Decision* at *11. Here, even assuming that the patent's "roadmap" provided guidance for making antibodies with binding properties similar to those of the working examples, no reasonable factfinder could conclude that there was adequate guidance beyond the narrow scope of the working examples that the patent's "roadmap" produced.

As the district court noted, the only ways for a person of ordinary skill to discover undisclosed claimed embodiments would be through either "trial and error, by making changes to the disclosed antibodies and then screening those antibodies for the desired binding and blocking properties," or else "by discovering the antibodies *de novo*" according to a randomization-and-screening "roadmap." *Id.* Either way, we agree with the district court that the required experimentation "would take a substantial amount of time and effort." *Id.* at *12. We do not hold that the effort required to *exhaust* a genus is dispositive. It is appropriate, however, to look at the amount of effort needed to obtain embodiments outside the scope of the disclosed examples and guidance. The functional limitations here

are broad, the disclosed examples and guidance are narrow, and no reasonable jury could conclude under these facts that anything but "substantial time and effort" would be required to reach the full scope of claimed embodiments.

We therefore conclude that, after weighing the *Wands* factors, the court did not err in concluding that undue experimentation would be required to practice the full scope of these claims.

Finally, Amgen is incorrect that the district court's decision is inconsistent with *Wands* or that our affirmance here would overrule *Wands*. *Wands*, as indicated above, does not hold that antibody screening never requires undue experimentation. The holding in *Wands* was based on the facts of that case and the evidence presented there. Here, the evidence showed that the scope of the claims encompasses millions of candidates claimed with respect to multiple specific functions, and that it would be necessary to first generate and then screen each candidate antibody to determine whether it meets the double-function claim limitations. *See Decision* at *7–13. The facts of this case are thus more analogous to those in *Enzo*, *Wyeth*, and *Idenix*, where we concluded a lack of enablement.

CONCLUSION

We have considered Amgen's remaining arguments but find them unpersuasive. For the reasons above, we affirm the district court's determination that the asserted claims are invalid for lack of enablement.

AFFIRMED

FORM 19. Certificate of Compliance with Type-Volume Limitations **Form 19**
July 2020

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATIONS

Case Number: 20-1074

Short Case Caption: Amgen Inc. v. Sanofi

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