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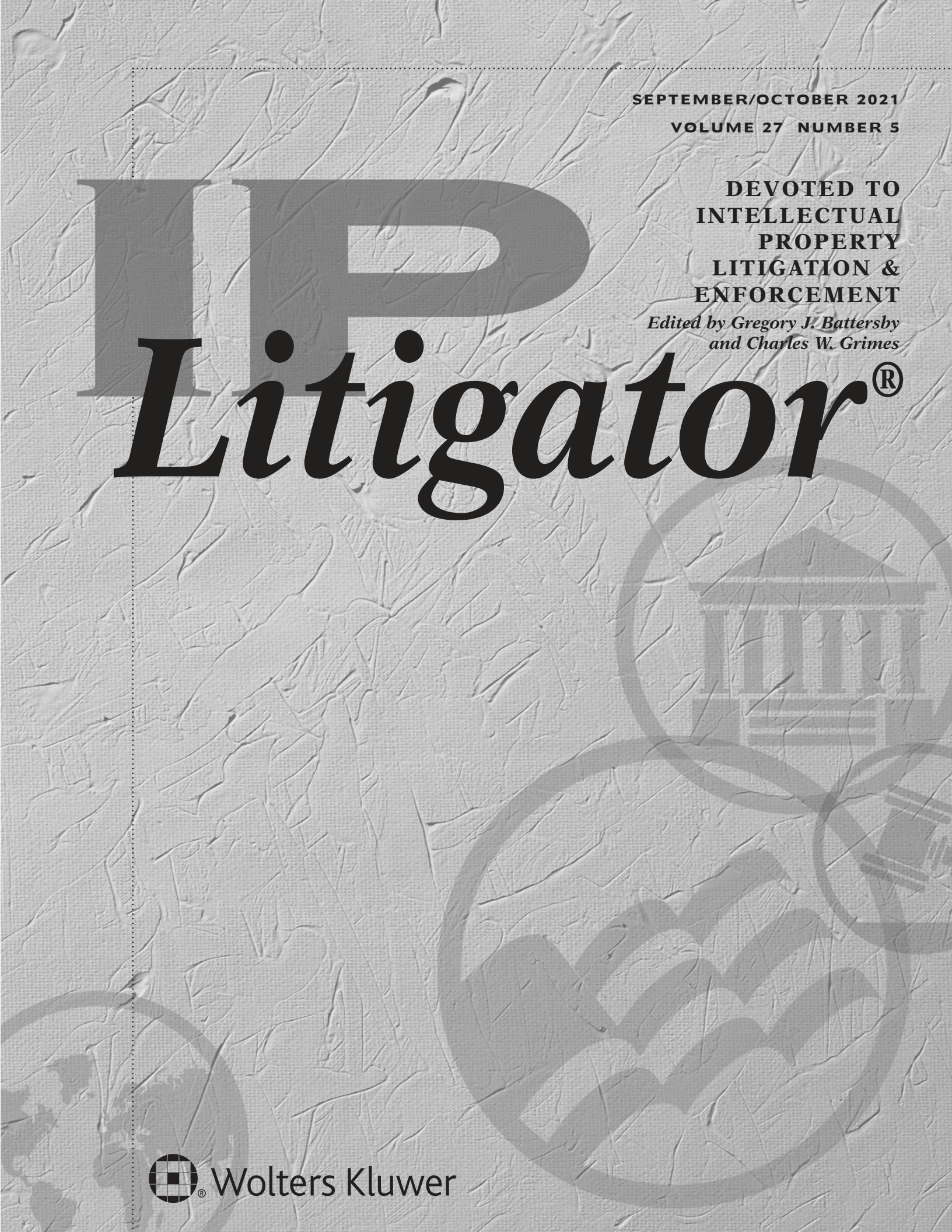

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Can Biopharma Functional Genus Patent Claims Be Resuscitated?

An en banc rehearing petition to the Federal Circuit seeks to breathe life back into the widespread practice of patenting a genus of compounds by claiming their common functional characteristics. This claiming practice was put on life support earlier this year when the Supreme Court denied certiorari in *Idenix v. Gilead*, a case that invalidated Idenix's functional genus claims under Section 112 of the patent statute.[1] The en banc petition, filed by Amgen in a long-running spat with Sanofi and Regeneron, argues that the Federal Circuit's heightened enablement standard under Section 112 improperly invalidates virtually any genus claim with functional limitations, and that enablement should be a question of fact, not law.[2] Whether Amgen's petition is successful has significant implications not only for Amgen but for the many biopharma companies who have similarly sought broad protection for their discoveries through genus claims containing functional limitations.

Idenix v. Gilead

In the *Idenix v. Gilead* case, the Federal Circuit held that Idenix's patent claims, which potentially covered a genus of billions of nucleosides said to be effective for treating hepatitis C, were invalid for lack of enablement and written description.[3] Through its certiorari petition, Idenix sought to reinstate a $2.5 billion patent damages award arguing, among other things, that the Federal Circuit improperly applied a bright-line, numbers-based enablement standard in finding its patented genus covered "too many" compounds.[4] According to Idenix's petition, the Federal Circuit's standard begs the question: "how 'many, many' is too 'many, many'?"[5] However, consistent with its apparent reticence to ruling on Section 112 issues, the Supreme Court denied certiorari.[6] Just a few weeks later, the Federal Circuit rendered its decision in *Amgen v. Sanofi*, affirming the invalidation of Amgen's patent for lack of enablement.[7]

Amgen v. Sanofi

Amgen's patent claims at issue cover a genus of monoclonal antibodies that purportedly bind to the protein PCSK9 and lower low-density lipoprotein (LDL) cholesterol levels by blocking PCSK9 from binding to LDL receptors.[8] The following patent claim is representative:

> 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 LDL[-]R.

The claimed antibodies thus were "defined by their function: binding to a combinations [sic] of sites (residues) on the PCSK9 protein, in a range from one residue to all of them; and blocking the PCSK9/LDLR interaction."[9] The patent specification disclosed the amino acid sequences for 26 antibodies, including the one marketed by Amgen as its cholesterol treatment, Repatha®.[10] After a jury found the patent claims were not shown to be invalid for lack of enablement and written description, and the district court denied JMOL, Sanofi appealed, and the Federal Circuit remanded the case for a new trial.[11] On remand, a second jury again found that Sanofi failed to prove that the asserted claims were invalid for lack of written description and enablement.[12] This time, however, the district court granted Sanofi's motion for JMOL of invalidity for lack of enablement, and Amgen appealed.[13]

On appeal, a panel of the Federal Circuit first stated that whether a claim satisfies the enablement requirement of 35 U.S.C. § 112 is a question of law based on underlying factual findings.[14] "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.'"[15] Among the factual considerations that must be weighed are the so-called *Wands* factors: (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.[16]

The court began by considering the *Wands* case itself.[17] The court noted that although the *Wands* decision upheld a claim to methods for the detection of hepatitis B surface antigen by using certain monoclonal antibodies, the case "did not proclaim that all broad claims to antibodies are necessarily enabled."[18] After examining its own precedent involving claims that include functional requirements, the court stated, "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." Turning to the case at bar, the court noted that Amgen's claims were composition claims defined, not by structure, but by meeting functional limitations, which "raises the bar for enablement."[19] The court concluded that Amgen failed to meet that heightened bar since its patent specification "did not enable preparation of the full scope of these double-function claims without undue experimentation."[20]

In reaching its conclusion, the court focused heavily on the eighth *Wands* factor, emphasizing that the claims were "broad" and that it was "not concerned simply with the number of embodiments [falling within the claims] but also with their *functional* breadth."[21] The court pointed out, for example, that there are three claimed residues to which no disclosed example binds.[22] The court stated it was "clear" that the claims were "far broader in functional diversity than the disclosed examples."[23] The Federal Circuit also highlighted the seventh *Wands* factor and agreed with the district court that antibody amino acid sequencing is an unpredictable field of science.[24] Amgen's expert witnesses themselves conceded that translating an antibody's amino acid "sequence into a known three-dimensional structure is still not possible," and "substitutions in the amino acid sequence of an antibody can affect the antibody's function, and testing would be required to ensure that a substitution does not alter the binding and blocking functions."[25] The court added that "while some need for testing by itself might not indicate a lack of enablement," here, there is "a conspicuous absence of nonconclusory evidence that the full scope of the broad claims can predictably be generated by the described methods."[26]

As for the second and third *Wands* factors, the Federal Circuit agreed with the district court 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."[27] The first *Wands* factor also weighed against Amgen, as "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."[28] Thus, "substantial time and effort would be required to reach the full scope of claimed embodiments."[29] The court elucidated that while it is not the effort required to "exhaust" a genus that matters, it is appropriate "to look at the amount of effort needed to obtain embodiments outside the scope of the disclosed examples and guidance."[30]

The Federal Circuit held that the district court "did not err in concluding that undue experimentation would be required to practice the full scope of these claims," and affirmed its finding of invalidity.[31]

Amgen's Rehearing Petition

Amgen argues that rehearing is required to resolve two areas of conflict with Supreme Court and Federal Circuit precedent.[32] First, the Federal Circuit "panel decision in this case announced a new and heightened standard for genus claims with functional limitations" that "evaluates the time and effort required to make and test every candidate so as to reach the full scope of *claimed embodiments*."[33] Second, the panel deemed enablement a question of law, reviewed without deference.[34]

According to Amgen, the panel's alleged new heightened standard defies precedent.[35] Under prior Federal Circuit precedent, "invalidity required concrete proof of an embodiment within the claims that was not enabled."[36] Under the Federal Circuit's new test, however, enablement is instead evaluated by "the effort to make and test each 'candidate' so as to identify every embodiment that meets the claimed function."[37] According to Amgen, the new test "does not examine the effort required to find any embodiment, but the effort to find every embodiment."[38] In Amgen's view, the new test conflicts with the Supreme Court's holding in *Minerals Separation*, for one, in which a patent "claimed improvements in the process for the concentration of a genus of ores by separating out non-metals," when there were "infinite varieties of ore."[39] The Supreme Court upheld the claim, explaining, "it is obviously impossible to specify in a patent the precise treatment for each variation," and it "was enough that POSAs could successfully apply the process to a particular ore."[40]

Amgen alleges the Federal Circuit's new enablement

standard also defies statutory text.[41] According to Amgen, "[b]ecause § 112 requires only that the specification enable POSAs to make and use the claimed invention, enablement asks whether the specification guides those skilled in the art to the successful application of the invention," which is "a standard of reasonableness."[42] Section 112 does not provide a "separate or heightened 'full scope of claimed embodiments' test for claims with functional limitations."[43]

Turning to policy, Amgen argues that the new standard threatens innovation, especially in biotechnology and pharmaceuticals.[44] "The central feature of patent law in the chemical, biotechnology, and pharmaceutical industries is the genus claim," but since "testing may be necessary to be 100% certain compounds function as intended, courts can now deem the effort to synthesize and screen candidates for the genus to be undue experimentation based on the potential number of candidates alone, even where POSAs would consider such work routine."[45] The result of the new standard is essentially that "[p]atents with functional limitations now lack enablement, no matter how routine it is to make any embodiment, simply because the genus is large."[46] The additional effort required to obtain genus claims will "consume[] scarce scientific resources better devoted to promoting progress."[47]

In its second main argument, Amgen urges the Federal Circuit to reconsider whether enablement is a question of law.[48] According to Amgen, for over 150 years, the Supreme Court recognized that enablement was a question of fact to be determined by the jury, until one day "[t]his 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)."[49] The distinction is important, Amgen argues, because here, the panel "cast aside the jury's implied findings under the guise of deciding a legal question."[50] The jury found "that Sanofi-Regeneron failed to prove, by clear-and-convincing evidence, that practicing Amgen's claims would require undue experimentation," but this court's view that enablement is a question of law, reviewed without deference, allowed the panel to reweigh the evidence.[51]

Conclusion

Amgen's petition raises fundamental questions about the balance between rewarding innovators with patent protection commensurate in scope with their initial discoveries in a particular area and reigning in overbroad functional claims, which disincentivize others from further innovating in that area. However, it is difficult to see where the impetus for the Federal Circuit to grant Amgen's petition will come from, particularly hot on the heels of the Supreme Court's denial of certiorari in *Idenix*, a case in which the Federal Circuit itself unanimously declined to rehear the case en banc. Perhaps Amgen's best shot will be another run at the Supreme Court in the hopes that the facts of its case are seen as a better vehicle for the Supreme Court to revisit enablement than those of the Idenix case. In the meantime, biopharma companies would be well served to revisit existing functional genus patent claims in their portfolios, and explore alternative claiming strategies, to maximize protection for their innovations.

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1. *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149 (Fed. Cir. 2019), *cert. denied*, 141 S. Ct. 1234 (2021).
2. Appellants' Pet. for Reh'g.
3. Brian Slater & Kiersten Fowler, *Are Biopharma Genus Patent Claims Dead?*, HAUGPARTNERS, (Dec. 8, 2020), *www.haugpartners.com/article/are-biopharma-genus-patent-claims-dead/*.
4. *See id.*
5. *Id.*
6. *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149 (Fed. Cir. 2019), *cert. denied*, 141 S. Ct. 1234 (2021).
7. *Amgen Inc. v. Sanofi (Amgen III)*, 987 F.3d 1080 (Fed. Cir. 2021).
8. *Id.* at 1083.
9. *Id.*
10. *Id.*
11. *Amgen Inc. v. Sanofi (Amgen I)*, 872 F.3d 1367, 1374, 1381–82 (Fed. Cir. 2017).
12. *Amgen Inc. v. Sanofi (Amgen II)*, No. 14-1317-RGA, 2019 U.S. Dist. LEXIS 146305, at *3, (D. Del. Aug. 28, 2019).
13. *Id.* at *51.
14. *Amgen III*, 987 F.3d at 1084.
15. *Id.* (citation omitted).
16. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

17. *Amgen III*, 987 F.3d at 1085.
18. *Id.* at 1085–86.
19. *Id.* at 1087.
20. *Id.*
21. *Id.* (emphasis in original).
22. *Id.*. at 1087 n.1.
23. *Id.* at 1087.
24. *Id.*
25. *Id.* (citations omitted).
26. *Id.* at 1087–88.
27. *Id.* at 1088 (citation omitted).
28. *Id.* (citation omitted).
29. *Id.*
30. *Id.*
31. *Id.*
32. Appellants' Pet. for Reh'g 12–13.
33. *Id.* at 12 (citations omitted) (emphasis in original).
34. *Id.* at 12.
35. *Id.* at 20.
36. *Id.* at 14 (citations omitted) (emphasis added).
37. *Id.*
38. *Id.* at 22 (emphasis in original).
39. *Id.* at 24 (citations omitted); *Minerals Separation, Ltd. v. Hyde*, 242 U.S. 261, 263 (1916).
40. Appellants' Pet. for Reh'g 24.
41. *Id.* at 23.
42. *Id.* (citations omitted).
43. *Id.* at 24.
44. *Id.* at 25–26.
45. *Id.* at 26 (citations omitted).
46. *Id.* at 23.
47. *Id.* at 27.
48. *Id.* at 28.
49. *Id.*
50. *Id.* at 29.
51. *Id.* at 29–31.

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