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CAFC Tightens Enablement Standard for Functional Claiming of Antibodies

Minding Your Business Blog on **March 15, 2021**

In the recent case of *Amgen Inc. v. Sanofi, Aventisub LLC*, the Federal Circuit affirmed the district court's invalidation of certain of Amgen's antibody patent claims, concluding that the claims were not "enable[d]" under 35 U.S.C. § 112. This decision establishes that it is more difficult to satisfy the enablement requirement for antibody claims that use functional language to describe the antibody. (The court granted Amgen's motion to extend the deadline for filing a petition for panel rehearing and/or rehearing en banc until April 14, 2021. *See id.*, Order (March 8, 2021).)

Antibody drugs represent a significant and expanding segment of pharmaceutical products, and pharmaceutical companies have waged high-stakes legal battles over antibody patents in an effort to retain control in the field of their therapeutic innovation.

The patent system's statutory *quid pro quo*, as interpreted by the courts, requires inventors to provide in their patent a written description of their invention that "enable[s] any person skilled in the art" to make and use the claimed invention without undue experimentation. *See* 35 U.S.C. § 112 and, *e.g.*, *In re Wands*, 858 F.2d 731, 733 and 737 (Fed. Cir. 1988). In *Amgen*, the Federal Circuit held that the district court did not err in finding that the patents at issue did not enable a person skilled in the art to make and use the the claimed inventions. *See Amgen*, 2021 WL 501114, at *6.

Specifically, the court affirmed the district court's judgment as a matter of law that the asserted patent claims were not "enabled," overturning the jury's conclusion. Amgen had asserted that Sanofi's Praluent® (alirocumab) product infringed certain claims of Amgen's U.S. Pat. Nos. 8,829,165 and 8,859,741, which covered Amgen's Repatha® (evolocumab) product. These antibody products target the naturally-occurring PCSK9 protein. By interfering with PCSK9 activity, these drugs help to lower LDL ("bad cholesterol"). (This post does not address other issues in the case such as infringement and other asserted bases for invalidity.)

The Federal Circuit applied the standard that "[w]hether 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." *Amgen* at *2. Section 112 provides "in relevant part that a patent's specification must 'enable any person skilled in the art … to make and use' the patented invention." *Id.* Further, disclosure must be "at least commensurate with the scope of the claims." *See id.* "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.'" *Id.* at *3.

The court analyzed enablement by evaluating the factors it had articulated in *Wands*: (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. *See id.* at *3. "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." *Id.* at *4.

The court focused on the breadth of the claims, including the number of candidate antibodies ("millions," *see id.* at *6) that the person of ordinary skill in the art would have to screen to determine whether each one met the claim-recited functional limitations, and on the functional breadth of the claims, noting, for example, that, although the claims include antibodies that bind up to sixteen residues, none of Amgen's patent examples binds more than nine (*see id.* at *5 n.1). The court thus gave weight to the defendants' position that undue experimentation depends on the number of theoretical candidates to be screened, and not on the actual number of species within the claimed genus, which Amgen had argued to be about 400 species (*see, e.g.*, Amgen's App. Br.:2-3).

The court also focused on unpredictability, noting that "this invention is in an unpredictable field of science with respect to satisfying the full scope of the functional limitations." *Id.* at *5. The court noted that the person of ordinary skill in the art cannot predict either a protein's three-dimensional structure from its amino acid sequence (*see id.* at *5) or the effects of amino acid substitution on antibody binding (*see id.* at *5). Consequently, the court held that even though the patent provided a procedural "roadmap" for producing antibodies such as those that the patents disclosed, the person of ordinary skill in the art still would need to discover undisclosed antibodies by trial and error or by using the roadmap, which would require "substantial time and effort." *See id.* at *6. In view of these considerations, the court affirmed the district court's judgment as a matter of law.

One may glean at least the following takeaways from *Amgen*. In view of the court's emphasis on the fact-specificity of enablement generally and on the procedural posture in this case specifically, and in view of the hazy nature of "undue experimentation," the court's application of the enablement requirement remains at least somewhat unpredictable. The court noted, for example, that "[w]e do not hold that the effort required to exhaust a genus is dispositive." *Id.* at *6. The court also stated with respect to *Wands*, which upheld as enabled claims that recited an antibody defined by function, that "*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." *Id.* at *4 and *see Wands*, 858 F.2d at 740 (reversing USPTO's Board of Patent Appeals and Interferences' rejection of applicant's claims).

Methods of claiming that are tied to antibody structure, rather than function, remain promising alternatives. However, the range of equivalents of such claims has not been fully tested. Applicants should continue to disclose, describe and claim embodiments of their invention in a variety of ways. Ultimately, patent applicants and patent owners will need a predictable enablement doctrine they can rely on during drug development, the patent application process, and in patent enforcement, whether that more predictable standard is articulated by courts or by Congress.

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