The patentability of antibodies in the United States

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Recent US case law attempts to further clarify the written description, novelty and nonobviousness requirements as they apply to antibodies

Two recent court cases, *Noelle v. Lederman* and *SmithKline Beecham v. Apotex*, shed light on the patentability of antibodies. The subtleties surrounding application of US patent statutes 35 USC §§ 102 (novelty and loss of right to patent), 103 (nonobvious subject matter) and 112 (specification) greatly affect the patentability of antibodies. To date, most of case law on this issue has revolved around the satisfaction of the requirements under Section 112.

Enablement

35 USC § 112 sets forth parameters that must be made by a patent application's specification in order to be considered patentable. The first paragraph of the statute sets forth the written description, enablement and best mode requirement and the second paragraph recites the requirement for definiteness. Although these requirements are tenets of patent law in general, the enablement requirement as it applies to antibodies was addressed in *Johns Hopkins University v. Cellpro, Inc.*, which held that the statute requires that the specification should "enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the [invention]"[1]. According to *Johns Hopkins*, "a person skilled in the art of making monoclonal antibodies must have a bachelor's degree in the appropriate scientific field and must have made a monoclonal antibody at least once"[2].

Through this decision, the US Court of Appeals for the Federal Circuit recognized that the requisite "ordinary skill" is actually a high level of skill in the field of antibodies. However, the Federal Circuit also imposed a high burden on "a party who wishes to prove that the claims of a patent are not enabled by means of a failed attempt to make the disclosed invention"—to do so the party "must show that the patent's disclosure was followed"[3].

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Written description

An additional facet of 35 USC § 112, first paragraph, is the written description requirement, which is separate and distinct from the enablement requirement. The purpose of the written description requirement is broader than to merely explain how to "make and use"; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention[4]. The Federal Circuit held in *Noelle v. Lederman* that "as long as an applicant has disclosed a 'fully characterized antigen,' either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen"[5]. This holding is consistent with the US Patent and Trademark Office (PTO) written description guidelines and is congruous with a previous decision wherein the Federal Circuit stated that "the PTO would find compliance with 112, 1, for a claim to an isolated antibody capable of binding to antigen X, notwithstanding the functional definition of the antibody, in light of the well-defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature"[6].

Therefore, the written description for an antibody is satisfied by fully characterizing an antigen so the antibody may be claimed by its binding affinity to that described antigen. Unfortunately for the plaintiff Noelle, the Federal Circuit held that he did not provide sufficient support for claims to a human antibody because he failed to disclose the structural elements of the human antibody or antigen. And, the court also held that Noelle was not entitled to the genus form of the antibody by simply describing the mouse antigen[7]. A take-home lesson of *Noelle v. Lederman* is that an antigen provides sufficient disclosure for an antibody claim; however, an antigen may not extrapolate to claims to an antibody genus.

Best mode

Currently, 35 USC § 112 also requires a "best mode contemplated by the inventor for carrying out his invention." *Evans Medical Ltd. v. American Cyanamid Company* held that "no biological deposit of a monoclonal antibody is necessary to comply with the best mode requirement of 35 USC § 112 because obtaining such antibodies was 'within ordinary skill'"[8]. However, *Evans* is an unpublished decision, so although the language in *Evans* appears beneficial to patent applicants, in reality, the effect of *Evans* will be minimal. Indeed, when *Evans* is considered in light of the case law encouraging the use of biological deposits to comply with the other portions of Section 112, applicants are left with the conclusion that deciding to forego a biological deposit is likely foolhardy.

The remaining portion of Section 112 provides that a patent is invalid for indefiniteness if it does not "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." The District of Columbia District Court held in *MorphoSys AG v. Cambridge Antibody Technology Limited* that a patent covering a method of obtaining antibodies to human self antigens for which specific antibodies were not found in the sera of humans was not invalid for indefiniteness, even if some testing was needed to determine whether any particular antibody came within scope of claims[9]. Unfortunately, the court

was not specific as to how much testing is too much, leaving applicants to guess at how much detail is required in their patent applications.

Novelty and nonobviousness

These recent court decisions have also had an impact on the patentability of antibody claims under 35 USC §§ 102 and 103, which provide that applicants are not entitled to a patent if the invention being claimed was anticipated or obvious in view of, among other things, the prior art. Many courts are recognizing that the issues surrounding whether or not an antibody is anticipated or obvious are complicated and varied, and are therefore refusing to rule on the issue as a matter of law[10]. The issue of novelty of antibodies could become more cantankerous if courts continue to follow the trend described in the dissent in *Smithkline Beecham v. Apotex*[11].

In *Smithkline Beecham*, the Federal Circuit granted a rehearing *en banc* for limited purposes, but in so doing upheld the lower court's "enlargement of the ground of invalidity called 'inherent anticipation'"[12]. Under this theory, it is now held that "a product that existed in trace amounts, although unknown and undetected and unisolated, is 'inherently anticipated' and barred from the patent system after it is discovered"[13]. As Justice Newman opines, antibodies are one area of research in which such a decision could have dire ramifications[14]. As antibodies themselves and the ability to generate such antibodies is inherent in a given species, it is entirely possible that such a doctrine would prohibit claims to the antibodies themselves as well as the antigens with which they interact. If such a construction of anticipation is overwhelmingly adopted, the only avenues for which patent coverage may be possible would be methods that, for example, provide new methods of isolation of the antibodies or new uses for the antibodies themselves. In either case, however, such claims would still likely face challenges of obviousness.

In view of the recent upsurge in litigations surrounding antibody patents and applications, applicants must be vigilant when preparing their applications to ensure they satisfy the requirements of 35 USC §112: too much description is likely better than not quite enough, and the use of biological deposits can only help in the quest for a patent. For now, applicants will have to wait for the determination of future cases for an answer as to whether "inherent anticipation" will void attempts to patent most antibodies and antigens. However, at this point, applicants have not received sufficient indications from the courts to prompt an abandonment of all attempts at the patenting of antibodies.

1. 35 USC § 112.
2. *Johns Hopkins University v. Cellpro, Inc.*, 152 F.3d 1342, 1360 (Fed. Cir. 1998) (quoting *Johns Hopkins University v. CellPro, Inc*., 931 F.Supp. 303, 323 (D. Del. 1996)).
3. *Id.* at 1360.
4. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563–1564 (Fed. Cir. 1991).
5. *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004).
6. *Id*. at 1349 (quoting *Enzo Biochem v. Gen-Probe, Inc*., 323 F.3d 956, 970 (Fed. Cir. 2002)).
7. *Id.* at 1350.
8. *Evans Medical Ltd. v. American Cyanamid Company*, 215 F.3d 1347, **1, 1999 WL 594310 (Fed. Cir. 1999).
9. *MorphoSys AG v. Cambridge Antibody Technology Limited*, 158 F.Supp.2d 84, 90-91 (D.D.C. 2001)).
10. For example, see *MorphoSys* at 89.
11. *Smithkline Beecham Corporation v. Apotex Corp*., 403 F.3d 1328 (Fed. Cir. 2005).
12. *Id.* at 1329 (Newman, J., dissenting).
13. *Id.* at 1330.
14. *Id.*