End of "well-characterised antigen" test?

THE CASE:
Amgen Inc v Sanofi
US Court of Appeals for the Federal Circuit
5 October 2017

A ruling followed by a patent office memo appears to have consigned to history the "well-characterised antigen" test for functional antibody claims, explains **Christopher E Loh**

35 USC § 112 of the United States patent statute requires that a patent provide a "written description of the invention" sufficient to reasonably convey that the inventors had possession of the claimed invention as of the patent's filing date. Whether a patent satisfies the written description requirement is a question of fact that depends on the nature of the claimed invention.

The written description requirement can present particular challenges with respect to patents that claim antibodies. Patent claims to antibodies can be expressed in functional terms (eg, "an isolated monoclonal antibody capable of binding protein X"), in structural terms (eg, "an isolated monoclonal antibody comprising the amino acid sequence of SEQ ID NO. 1") or using a combination of structural and functional terms.

Guidance issued in the early 2000s from the United States Patent and Trademark Office ("USPTO") suggested that antibody claims expressed in purely functional terms could satisfy the written description requirement if the antigen to which the antibodies bound was sufficiently "well-characterised". However, more recent developments – in particular, the US Court of Appeals for the Federal Circuit's 5 October 2017 decision in *Amgen Inc v Sanofi*[1] – have cast doubt upon the continued vitality of that guidance.

The test's origin

In 2000, and again in 2008, the USPTO published *Written Description Training Materials* for its patent examiners teaching that a purely functional antibody claim, eg, "an isolated antibody capable of binding to antigen X," could satisfy the written description requirement if the patent specification described antigen X by its amino acid sequence, its physical properties, and the methods by which it was isolated and purified – even if the specification omitted any detailed description or working examples of the antibodies themselves.[2] According to the USPTO training materials, such an outcome would be warranted in circumstances where, "the level of skill and knowledge in the art of antibodies at the time of filing was such that production of antibodies against a well-characterised antigen was conventional."[3]

Initially, the Federal Circuit seemed receptive to adopting the USPTO's above "well-characterised antigen" test. In *Enzo Biochem, Inc v Gen-Probe Inc*[4] the Federal Circuit, sitting *en banc*, reversed a district court's summary judgment that Enzo's patent claims were invalid for failure to meet the written description requirement. The patent claims in *Enzo* were directed to nucleic acid probes that bound the DNA of the bacteria *N gonorrhoeae* over the DNA of the bacteria *N meningitides* by a ratio "greater than about five". Relying in part upon the USPTO's "well-characterised antigen" guidance, Enzo argued to the Federal Circuit that the claims met the written description requirement because, among other things, the patent clearly identified the strains of *N gonorrhoeae* and *N meningitides* to which the claimed probes bound.[5] The Federal Circuit agreed with Enzo that, in view of the USPTO's "well-characterised antigen" guidance, the identification in the patent of the bacterial strains to which the claimed probes bound was sufficient at least to foreclose summary judgment of invalidity due to inadequate written description. According to the Federal Circuit in *Enzo*, "Because the claimed nucleotide sequences preferentially bind to the genomic DNA of the deposited strains of *N gonorrhoeae* and have a complementary structural relationship with that DNA, those sequences, under the USPTO Guidelines, may also be adequately described… Such hybridisation to disclosed organisms may meet the USPTO's Guidelines stating that functional claiming is permissible when the claimed material hybridises to a disclosed substrate.[6]

Retreat from "well-characterised antigen" test

The Federal Circuit's post-*Enzo* treatment of the "well-characterised antigen" test, however, has been progressively less favourable.

In *Noelle v Lederman*,[7] the Federal Circuit held that Noelle's earlier-filed patent application failed to satisfy the written description requirement with respect to Noelle's later-filed functional claims to antibodies that bind human CD40CR, or CD40CR proteins generally. The Federal Circuit reasoned that the earlier-filed application described only mouse CD40CR; that the earlier-filed application did not disclose human CD40CR or other CD40CR proteins; and that application of the USPTO's "well-characterised antigen" test was limited to circumstances in which a patent "has disclosed a 'fully-characterised antigen,' either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository."[8]

In *Centocor Ortho Biotech, Inc v Abbott Labs*,[9] the Federal Circuit shifted focus from the antigen to the antibodies themselves.

The patent claims at issue in *Centocor* were directed to fully human antibodies that bind human TNF-α with high affinity, neutralising activity and A2 specificity. Relying in part upon the USPTO's "well-characterised antigen" guidance, Centocor argued to the Federal Circuit that the description in its earlier-filed application of human TNF-α provided an adequate written description of any antibody that bound human TNF-α.[10] The Federal Circuit disagreed, holding that the USPTO's "well-characterised antigen" test was limited to circumstances in which "(1) the applicant fully discloses the novel [antigen] protein and (2) generating the claimed antibody is so routine that possessing the protein places the applicant in possession of an antibody."[11] As to the second factor, the Federal Circuit found that obtaining a high-affinity, neutralising, A2 specific fully human antibody was not possible using conventional or routine technology available as of the date of Centocor's earlier-filed application.[12]

Amgen v Sanofi Decision

In *Amgen Inc v Sanofi* the Federal Circuit held that a district court erred in instructing a jury that the written description requirement could be satisfied, as to Amgen's functional antibody claims, "by the disclosure of a newly-characterised antigen…if you find that the level of skill and knowledge in the art of antibodies at the time of filing was such that production of antibodies against such an antigen was conventional or routine."[13] The Federal Circuit's rejection of the jury instruction in *Amgen* is surprising, given that the instruction follows the Federal Circuit's determination in *Centocor* that the USPTO's "well-characterised antigen" guidance should apply where the applicant fully discloses the novel antigen, and generating an antibody to that antigen is considered sufficiently routine that possessing the antigen places the applicant in possession of an antibody.[14] The Federal Circuit in Amgen nevertheless proceeded to distinguish *Centocor* – as well as *Noelle* and *Enzo* – noting that in *Centocor* and *Noelle*, the antibody claims ultimately were held invalid for lack of adequate written description notwithstanding the USPTO's guidance, and that in *Enzo*, the claims concerned nucleic acids rather than antibodies and the references to the USPTO's guidance there were mere dicta.[15]

The Federal Circuit in *Amgen* further explained that "the essential problem" with the jury instruction was that it contradicted long-standing precedent that, "to satisfy the statutory requirement of a description of the invention, it is not enough for the specification to show how to make and use the invention, ie, to enable it."[16] The Federal Circuit continued, "[T]he "newly characterised antigen" test flouts basic legal principles of the written description requirement. Section 112 requires a "written description of the invention".

But this test allows patentees to claim antibodies by describing something that is not the invention, ie, the antigen. The test thus contradicts the statutory '*quid pro quo*' of the patent system where one describes an invention, and, if the law's other requirements are met, one obtains a patent.[17]

Despite these seemingly broad pronouncements, the Federal Circuit's 2017 *Amgen* decision noted that each case involving the issue of written description "must be decided on its own facts" and thus that the precedential value of written description cases is "extremely limited."[18] The Federal Circuit also observed that "we cannot say that this particular context, involving a 'newly characterised antigen' and a functional genus claim to corresponding antibodies, is one in which the underlying science establishes that a finding of 'make and use' (routine or conventional production) actually does equate to the required description of the claimed products."[19] In view of those caveats, the Federal Circuit perhaps may have left open the door for the application of the "well-characterised antigen" test in other contexts.

The USPTO appears less sanguine about prospects for the "well-characterised antigen" test. On 22 February, 2018, it issued a memorandum to its examiners stating that, "[i]n view of the *Amgen* decision, adequate written description of a newly characterised antigen alone should not be considered adequate written description of a claimed antibody to that newly characterised antigen, even when preparation of such an antibody is routine and conventional."[20] The USPTO memo further advises that the 2000 and 2008 training materials are, "outdated and should not be relied upon as reflecting the current state of the law," and that its *Manual of Patent Examining Procedure* (MPEP) § 2163 should not be followed "insofar as MPEP 2163 indicates that disclosure of a fully characterised antigen may provide written descriptive support of an antibody to that antigen."[21]

Summary

The Federal Circuit's 2017 *Amgen* decision and the USPTO's 2018 memo would appear to spell the end of the "well-characterised antigen" test in the US. According to *Amgen*, application of the test would run afoul of the written description requirement by "allow[ing] patentees to claim antibodies by describing something that is not the invention, ie, the antigen." Thus, going forward, US patentees should no longer count upon a description of an antigen by itself to constitute an adequate written description under 35 USC § 112 of functional claims to antibodies that bind that antigen. This is in contrast with the policy of the European Patent Office, which generally considers functional claims to an antibody that binds an antigen to be "sufficient" if the antigen is novel, and the antibody can be generated using standard or routine techniques.[22] (European patent law, however, does not impose a written description requirement separate from the sufficiency requirement.)

Nevertheless, the *Amgen* decision itself notes that each written description case must be decided on its own facts, thereby giving rise to the possibility that some form of the "well-characterised antigen" test might apply under other facts. What other facts may permit application of the test remains to be seen.

Footnotes

1. 872 F.3d 1367 (Fed Cir 2017).
2. See USPTO *Written Description Training Materials* (Rev 1 Mar 25 2008), pp 45-46. https://www.uspto.gov/sites/default/files/web/menu/written.pdf
3. Id at p. 46.
4. 323 F.3d 956 (Fed Cir 2002).
5. Id at 964, 967-68.
6. Id at 968.
7. 355 F.3d 1343 (Fed Cir 2004).
8. Id at 1349 (emphasis in original).
9. 636 F.3d 1341 (Fed Cir 2010).
10. Id at 1351.
11. Id at 1352.
12. Id at 1353.
13. Id at 1372.
14. 636 F.3d at 1352.
15. 872 F.3d at 1376-77
16. Id at 1378.
17. Id at 1379.
18. Id at 1361.
19. Id at 1362.
20. See https://www.uspto.gov/sites/default/files/documents/amgen_22feb2018.pdf
21. Id.
22. See, eg, Holliday, L, *Patenting antibodies in Europe, mAbs* 1:4, 385-386 (July/Aug 2009).

Author

Christopher E Loh is a partner at Fitzpatrick, Cella, Harper & Scinto, an experienced litigator and an award-winning author of publications on a range of intellectual property issues.