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Treatment of Antibody Claims In the U.S. After 'Amgen v. Sanofi'

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The future of antibody claiming in the United States is uncertain following the U.S. Supreme Court's May 2023 ruling in *Amgen Inc. v. Sanofi,* 598 U.S. 594 (2023), a highly anticipated decision concerning enablement and whether the traditional way to claim antibodies — claiming antibodies by their function — will survive as a valid claiming strategy.

Since the *Amgen* decision and as of November 2023, the case has been cited in seven Patent Trial and Appeal Board (PTAB) decisions, seven district court cases and three federal circuit cases. Of those, three focused on antibodies.

To recap, the U.S. Supreme Court held in *Amgen* that claims 19 and 29 of Amgen's '165 patent (U.S. Patent No. 8,829,165) and claim 7 of their '741 patent (U.S. Patent No. 8,859,741) were invalid for lack of enablement.

Claim 19 of the '165 patent reads:

"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."

Claim 29 of the '165 patent reads:

“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 blocked the binding of PCSK9 to LDLR by at least 80%.

Claim 7 of the ‘741 patent reads:

“The isolated monoclonal antibody of claim 2, wherein the epitope is a functional epitope.”

Both Amgen and Sanofi had developed and sought patent protection for antibodies that function to inhibit a protein known as PCSK9, which helps to lower LDL-cholesterol in humans. Amgen had successfully isolated and produced the amino acid sequences of 26 PCSK9-inhibiting antibodies but sought to claim the entire genus of possible antibodies that could perform the same inhibiting function. On this basis, Amgen alleged that Sanofi’s antibody infringed their patents.

The Supreme Court disagreed, reasoning that where a patent claims an entire class of processes, machines, manufactures, or compositions of matter, the patent’s specification must enable a person skilled in the art to make and use the entire class. In short, “[t]he more one claims, the more one must enable.” *Amgen* at 610.

While Amgen had properly enabled the 26 antibodies disclosed by amino acid sequence, it had left the remainder of the vast antibody genus up to a trial-and-error experimentation process, which the Court likened to a hunting license. Additionally, Amgen had not identified a quality common to all of the antibodies that gave them “a peculiar fitness for that particular purpose” in the claimed genus, which the Court said may, in another instance, reliably enable a person skilled in the art to make and use all of what is claimed and not just a subset.

The cases following Amgen have attempted to further clarify the enablement requirement. The bulk of opinions at all levels from PTAB to the federal circuit focusing on determining the scope of the claims at issue and whether a person skilled in the art would need to undergo undue experimentation to practice that full scope. However, three cases have emerged which have called into question the means by which antibodies may be claimed in the future, if at all.

In re Xencor, Inc.

In June 2023 the PTAB issued a decision rejecting a request for rehearing by Xencor on their patent application directed to antibodies for the treatment of autoimmune conditions. *See*, Brief of Appellant, *In re Xencor, Inc*., No. 2023-2048 (Fed. Circ. Sept. 29, 2023). Xencor's claims had been written in the means-plus-function format and disclosed at least one corresponding structure with which to perform the means in the specification. Despite noting that they were unaware of any case law on means-plus-function claims for antibody patents, the Board rejected the claims, finding that Xencor had not described the structural equivalents of the antibody disclosed—of which there could be a vast number.

The Board did not cite *Amgen* in their decision, and instead based its rejections on its interpretation of §112(f), finding the claimed antibodies to be members of a chemical genus. If affirmed on appeal at the Federal Circuit, the case could remove much of the remaining ability of practitioners to appropriately claim antibodies in the means-plus-function format, which was one of the few viable options remaining in the wake of *Amgen*.

The American Intellectual Property Association (AIPLA) and several other firms and individuals have filed briefs on Xencor's behalf, urging the Federal Circuit to keep means-plus-function claiming intact and to overrule the decision by the PTAB.

Baxalta Incorporated v. Genentech, Inc.

In September 2023 the Federal Circuit affirmed a district court's grant of summary judgment that Baxalta's patent (U.S. Patent No. 7,033,590) was invalid for lack of enablement. *See*, *Baxalta Inc. v. Genentech, Inc*., 81 F.4th 1362 (Fed. Cir. 2023). Baxalta's patent claimed antibodies that could be used to treat Hemophilia A and disclosed the amino acid sequence of 11 such antibodies.

Independent claim 1 is representative:

"An isolated antibody or antibody fragment thereof that binds Factor IX or Factor IXa and increases the procoagulant activity of Factor IXa."

Applying *Amgen*, the Federal Circuit found that Baxalta sought to claim an entire genus of antibodies, but only disclosed 11 antibodies by amino acid sequence, and provided a roadmap that would require researchers to engage

in undue experimentation. The court additionally found that Baxalta did not explain why the 11 disclosed antibodies worked for their intended purpose while others would not, and had not disclosed a quality common to every functional embodiment, as required by the interpretation of enablement set forth by *Amgen*, so that a skilled artisan could predict which antibodies — after following Baxalta's roadmap — would perform the claimed functions.

Note well that the Federal Circuit did use this case to affirmatively state that they do not interpret *Amgen* to disturb the *In re Wands* enablement test or its factors.

Teva Pharmaceuticals v. Eli Lilly

Most recently, in September 2023, the District Court for the District of Massachusetts heard a dispute between Teva Pharmaceuticals and Eli Lilly where Lilly alleged that Teva's patents (U.S. Patent No. 8,586,045, U.S. Patent No. 9,884,907, and U.S. Patent No. 9,884,908) directed to a method for the treatment of certain headache disorders by administering an antibody were invalid for lack of enablement. *See*, *Teva Pharm. Int'l GMBH v. Eli Lilly & Co.*, Civil Action No. 18-cv-12029-ADB, 2023 U.S. Dist. LEXIS 171953 (D. Mass. Sep. 26, 2023).

Claim 1 of the '907 patent is representative:

1. A method for treating headache in an individual, comprising:

administering to the individual an effective amount of a humanized monoclonal anti-Calcitonin Gene-Related Peptide (CGRP) antagonist antibody, comprising:

two human IgG heavy chains, each heavy chain comprising three complementarity determining regions (CDRs) and four framework regions, wherein portions of the two heavy chains together form an Fc region; and

two light chains, each light chain comprising three CDRs and four framework regions;

wherein the CDRs impart to the antibody specific binding to a CGRP consisting of amino acid residues 1 to 37 of SEQ ID NO:15 or SEQ ID NO:43.

Teva described 97 antibodies and antibody fragments in their specification by structure, and, like in *Amgen*, provided a process by which a person skilled in the art might isolate antibodies with a similar function.

The district court applied both *Amgen* and *Baxalta*, holding that a reasonable jury could have found that Teva Pharmaceuticals' claims were broad enough to encompass the entire functionally-defined genus of antibodies of which the actual number of antibodies in that genus is unknowable, and that their isolation process would create a burden of undue experimentation for anyone seeking to make and utilize similar antibodies, even if the experimentation itself were considered routine.

What Now?

Going forward it seems that the best option for practitioners moving forward is to ensure several things in their application drafting process.

First, educate inventor(s) about the present uncertainty around antibody claiming in the U.S. and obtain as many embodiments and common qualities as reasonably possible.

Second, describe with particularity those embodiments, preferably in both structure and function and a mix of both, in the specification.

Third, if possible, describe any common quality(s) among all of the antibodies besides binding an antigen.

Lastly, while U.S. law is still uncertain on antibody claiming, protect antibodies using several different claim types with varying scope, such as: functional-only claims (for outside the U.S. protection), structural-only claims, function-plus-structure claims, method claims, means-plus-step claims, means-plus-function claims, device claims, kit claims and composition claims.

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