Professional Perspective

Challenges of 'Enabling' Antibody Claims with Functional Limitations

Jonathan B. (J.B.) Fitzgerald, Charles F. Hauff, and Jeffrey D. Morton

Bloomberg Law

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Contributed by Jonathan B. (J.B.) Fitzgerald, Charles F. Hauff, and Jeffrey D. Morton, Snell & Wilmer

Synthetic antibodies have become an important aspect in the development of novel therapeutics. Since the 1980s, hundreds of antibodies have been designed as drugs. Thus, many biopharmaceutical companies have and continue to make significant research and development investments in developing synthetic antibodies.

To protect their investments, companies often seek patent protection to cover the synthetic antibodies they have developed and key aspects related to those antibodies. Broad genus patent claims that cover the antibodies, and variants of the antibodies, are often ideal as these types of claims can be more effective in preventing easy design arounds by competitors. A recent Federal Circuit case illustrates the challenges companies may encounter when seeking broad claims to protect their synthetic antibodies.

Amgen v. Sanofi - Enablement Analysis of Amgen's Antibody Claims

In *Amgen v. Sanofi*, the Federal Circuit struck down Amgen's antibody claims because the court found that the claims failed to meet the enablement requirement. *Amgen v. Sanofi*, Appeal No. 2020-1074 (Fed. Cir., 2021). In its enablement analysis, the Federal Circuit focused on the issue of whether undue experimentation would be required to make and use Amgen's claimed antibodies. The court found that it would.

Amgen's Functionally Directed Antibody Claims

Instead of claiming structural features, such as the sequences of the antibodies, Amgen's antibodies were claimed by setting forth two functional limitations. The first was that the antibodies were capable of binding specific amino acid residues on the PCSK9 protein, a known target in reducing high cholesterol.

The second was that the antibodies were capable of blocking binding of PCSK9 to the low-density lipoprotein receptor (LDLR), thus, carrying out the therapeutic effect of the antibodies. Accordingly, the antibodies were functionally claimed according to their therapeutic functions of binding specific amino acid residues on a protein (PCSK9) and preventing binding of that protein to a specific receptor (LDLR). This claim approach is typical and widely used.

Analysis of the "Functional Breadth" of Amgen's Antibody Claims

Because Amgen's antibody claims recited functional features of the antibodies, instead of structural features, the Federal Circuit evaluated whether the "functional breadth" or functional diversity of the claims was enabled by the guidance in the specification. Specifically, the court analyzed whether the full scope of the antibodies covered by the claims could be predictably generated based on the examples set forth in the patent specification, without undue experimentation.

In carrying out this analysis, the Federal Circuit noted that antibodies are part of a field that is unpredictable. Additionally, an expert for Amgen testified that sequence substitutions in an antibody can affect the antibody's function and, thus, testing would be needed to determine whether a substitution altered the antibody's binding and blocking functions. Further, according to the court, the specification provided little to no evidence, other than conclusory evidence, that the full scope of the antibodies covered by the claims could predictably be generated by the disclosed examples.

Thus, the Federal Circuit concluded that the guidance in the specification was sufficient only to predictably generate a subset of antibodies covered by the claims. As a result, the court found that undue experimentation would be required for a person of skill to practice the full scope of the claims. This undue experimentation, according to the court, would require an extensive trial and error process of synthesizing and screening the antibodies to determine whether they were capable of binding to the proper residues of PCSK9, and preventing binding of PCSK9 to LDLR.

On this basis, the Federal Circuit affirmed the lower court's decision that the claims were invalid due to failure to meet the enablement requirement.

Challenges of Protecting Functional Antibody Genus Claims

You can more readily track litigation data if it is built from pre-populated, standardized input values—think multiple choice rather than free text. This will reduce the "noise" from typos, minor language changes, and differences in convention. For instance, you might use a single input value for "Response/Opposition to Motion for Summary Judgment" rather than the many other ways this document could be referred to in a free text field.

Where possible, you should explore compiling data from existing platforms such as document databases or other case management programs. This will reduce the lift of attorneys' manual data input. However, even when data is sourced from existing programs, budget adequate time to standardize the data for your analysis. In the example above, "Response/Opposition to Motion for Summary Judgment" documents may be saved under varying filenames in a document database. Individualized review is necessary to make the data actionable for litigation analysis.

If there is no existing data to work from, input will come from practitioners responsible for day-to-day management of the litigation matter. This may be very time-consuming depending on the number of stakeholders. You should carefully consider workflow and minimize the disruption of the data input—for example, by engaging non-attorneys.

Issues with 'Double-Function' Antibody Claims and 'Binding Limitations'

The *Amgen* court made specific reference to "double-function" antibody claims, referring to the dual function of Amgen's claimed antibodies that are capable of both binding specific residues on a protein, and preventing binding of the protein to a receptor. The court stated that the "binding limitation" in the claims would be sufficient for a finding of undue experimentation. This emphasis may have had to do with a concession by one of Amgen's experts that amino acid sequence substitutions in an antibody can alter the binding properties of the antibody.

These references to "double-function" antibody claims and the "binding limitations" could be signals of caution from the Federal Circuit. Specifically, it may suggest that any future antibody claims that come before the Federal Circuit that attempt to claim the antibodies according to dual functional characteristics related to binding properties will be heavily scrutinized under the enablement requirement.

Claiming Structural Features of Antibodies

To potentially avoid issues from functionally claiming antibodies that could arise due to the *Amgen* case, one possible strategy may be to claim structural features of the antibodies. One structural claiming option is to claim the entire antibody sequence, but this option may result in antibody claims that are narrow in scope, and, thus, easy to design around by competitors. This issue can be ameliorated, to some degree, by claiming a percent identity of the antibody sequence that is less than 100%.

An alternative structural claiming option is to claim regions or sequences of the antibodies that are known to be important in antibody/epitope binding. These might include claiming antibody variable regions, which are regions of antibodies that are responsible for the specificity of an antibody to a given epitope; complementarity-determining regions (CDRs), which are regions within variable regions that are responsible for direct contact between an antibody and an epitope; or "consensus" sequences within CDRs, which are sequences that are known to be critical in the establishment of the antibody/epitope interface.

The *Amgen* case demonstrates the challenges that protecting broad, functional antibody genus claims will pose. As such, companies should carefully consider strategies when attempting to protect their synthetic antibodies. If a company chooses to protect its antibodies through functional claiming, it likely will be beneficial to evaluate whether enough data and methods have been demonstrated to enable the "functional breadth" of the claims. Alternatively, a company may consider claiming the structural features of the antibodies.

Going forward, consulting with counsel on strategies related to protecting synthetic antibodies may be useful to companies in navigating any issues implicated by the *Amgen* case. Also, as part of a comprehensive strategy for patenting their antibodies, companies may consider the jurisdictions in which they want patent protection, as well as any differences amongst the jurisdictions regarding the requirements for patenting such antibodies.