Keywords: enablement; *Wands* factors; antibody claims, functional language, undue experimentation

General: Functional limitations in a claim to a composition of matter may result in claim breadth that is not fully enabled if undue experimentation is required to determine the scope of the functional limitations.

Amgen Inc. v. Sanofi
United States Court of Appeals for the Federal Circuit
No. 2020-1074
Decided February 11, 2021

I. Facts

Amgen owns U.S. Patent Nos. 8,829,165 ("the '165 patent") and 8,859,741 ("the '741 patent"), which cover Amgen's Repatha™ therapy for high cholesterol. The '165 patent and the '741 patents share a common specification and generally describe antibodies that are specific for an enzyme, PCSK9. The antibodies bind and disrupt the normal action of PCSK9 to degrade LDL receptors, and this ultimately results in more available LDL receptors that can bind LDL cholesterol and remove LDL cholesterol from the blood stream. The specification discloses amino acid sequences for twenty-six different antibodies, including the antibody that is sold as Repatha™.

Amgen sued Sanofi and Regeneron (collectively "Sanofi") on October 14, 2014, for infringing the '165 patent and the '741 patent over sales of Praluent®, which competes with Amgen's Repatha™.

Certain relevant claims in the '165 patent are:

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.
>
> 19. 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.

Relevant claims in the '741 patent is:

> 1. An isolated monoclonal antibody that binds to PCSK9, wherein the isolated monoclonal antibody binds an epitope on PCSK9 comprising at least one of residues 237 or 238 of SEQ ID NO: 3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.

> 2. The isolated monoclonal antibody of claim 1, wherein the isolated monoclonal antibody is a neutralizing antibody.
> 7. The isolated monoclonal antibody of claim 2, wherein the epitope is a functional epitope.

In the first trial, Sanofi stipulated to infringement of claims 19 and 29 of the '165 patent and claim 7 of the '741 patent, and the jury determined that the '165 patent and the '741 patent were enabled and had adequate written description. Sanofi appealed to the Federal Circuit, and the Federal Circuit held that the district court erred in evidentiary rulings and jury instructions regarding defenses that the '165 patent and the '741 patent lack enablement and written description. On remand, a second jury found that the '165 patent and the '741 patent were enabled and had adequate written description. The district court granted Sanofi's motion for judgment as a matter of law for lack of enablement and denied its motion for lack of written description. Amgen appealed to the Federal Circuit.

II. Issue

Are the asserted claims of the '165 patent and the '741 patent enabled?

III. Discussion

No. The Federal Circuit affirmed district court's holding that a person of ordinary skill in the art would not be able to practice the claimed invention without undue experimentation. The Federal Circuit panel weighed the *Wands* factors in a fact-based analysis in considering whether the claims were enabled:

> (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
> (8) the breadth of the claims

Amgen argued that, under the *Wands* factors, there is no undue experimentation require to obtain antibodies within the scope of the claims. Amgen presented expert testimony that the specification provided a "roadmap" to make all of the antibodies within the scope of the claims. Amgen also argued that the district court incorrectly interpreted the enablement requirement as encompassing the effort to make every possible embodiment of the claims and also argued that Sanofi failed to provide any examples of embodiments outside of the teaching of the specification.

Sanofi argued that there are millions of potential antibody candidates within the scope of the claims because the functionally-defined claims cover a vast scope, antibody generation is unpredictable, and that a great deal of trial and error would be necessary. Sanofi also pointed out that all of Amgen's arguments were limited to breadth and number of the known antibody candidates in the specification, but that the enablement requirement required examining the number of candidates that must be made and tested.

The Federal Circuit agreed with Sanofi, noting that "[w]hile functional claim limitations are not necessarily precluded in claims that meet the enablement requirement, such limitations pose high hurdles in fulfilling the enablement requirement for claims with broad functional language." The Federal Circuit pointed to the claim language itself as defining a functionally broad class of antibodies that "are far broader in diversity than the disclosed examples." For example, certain claims recited binding to "at least one of" sixteen different amino acids, and none of the disclosed examples bound to more than nine, and none of the disclosed example bound to three of the amino acids at all.

IV. Conclusion

The use of functional language in a claim may raise the bar for an enabling disclosure, particularly in less predictable arts.