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NEWS

The CAFC's *Amgen v Sanofi* decision spells trouble for broad functional patent claims

The CAFC's much-anticipated ruling has major implications for antibody patents and continues the court's trend of imposing a tough enablement standard for genus claims

The end of last week saw the US Court of Appeals for the Federal Circuit hand down a highly significant decision in *Amgen v Sanofi* – the latest development in the much-watched international patent dispute regarding the use of PCSK9 inhibitors to lower cholesterol.

Upholding a 2019 district court finding that two broad, functionally-defined, antibody patents belonging to Amgen are invalid for lack of enablement, the judgment is a big blow to the Californian company, which alleged that Sanofi's rival PCSK9 inhibitor drug, Repatha, infringes its IP rights.

But the decision also has a much broader significance, developing US enablement case law and making clearer the patent requirements that must be met by innovators in the increasingly important antibody space.

Here are the main takeaways from the ruling.

This was an important test case for functionally-defined antibody genus claims

"The case has major implications for our case law in terms of what kinds of functional field or genus claims can be obtained," explains Dechert's Katherine A. Helm. "Functional genus claims have long existed, but the *Amgen* case raised a spectre of uncertainty surrounding what functional language can be used to claim a broad genus of antibodies."

To meet the enablement requirement, patents need to teach the skilled person how to practise the claimed invention across its breadth without undue experimentation.

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In this case, the Federal Circuit reviewed the invalidation of Amgen's US patents '165 and '741, which claim antibodies that bind to the PCSK9 protein and lower LDL cholesterol levels by preventing PCSK9 from binding to LDL receptors. Though the specification discloses amino acid sequences for 26 specific antibodies in the genus, this functional claim covers many thousands if not millions of potential antibodies.

Arguments before the Federal Circuit centred on whether Amgen's rights passed the paradigmatic *Wands* test for determining whether undue experimentation is required. This involves the weighing of eight factual considerations, including: the quantity of experimentation necessary; the amount of guidance presented in the patent; the nature of the disclosed working examples; the unpredictability of the art; and the breadth of the claims.

Amgen claimed that, despite the large number of potential antibodies covered, no undue experimentation is required, because the patent provides a roadmap using anchor antibodies and well-known screening techniques which can be used to make all antibodies within the patent's scope. It contended that the lower court had erred by failing to factor in Sanofi's failure to identify any single antibody that could not be made. Also, pointing out that the disclosed embodiments were deemed representative enough of the claims genus to satisfy the written description requirement, it said that this was sufficient to establish structure/function correlation for enablement.

The company also suggested that the *Wands* precedent itself – in which methods of using functionally-defined antibodies were found to be enabled – supported its broad antibody claims.

Such claims are now difficult (though not impossible) to uphold

The Federal Circuit rejected Amgen's arguments, finding that *Wands* did not mean that all broad antibody claims are necessarily enabled; the facts of this case differed from those of *Wands*.

It stressed that enablement inquiries for functional claims "can be particularly focused on the breadth of the claims, especially where predictability and guidance fall short". The functional diversity of the claimed embodiments exceeded that of the examples disclosed by the patents, the court found; and there was only evidence to suggest a small subset of antibodies could be reliably generated. No reasonable jury could find that "substantial time and effort" for further experiment was not due in this case.

"The court has held that functional limitations – and in this case double-functional limitations – impose a high hurdle for enablement," comments Irena Royzman of Kramer Levin. "The bottom line is that for antibodies, functional limitations set the bar higher, so that is something to be aware of when writing patents. The decision makes clear that you cannot own an antibody target."

"Once you start talking about tens of thousands, up to millions of possible compounds and unpredictable art, the case for enablement is more difficult to make," says Matthew Wolf of Arnold & Porter, who represented Sanofi in the case.

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“Functional claiming is permissible as long as there is a predictable relationship between structure and function. If there isn't, then it's hard to functionally claim.”

This structure-function relationship is much easier to establish for a chemical compound, Helm explains: “In antibodies, it is difficult to establish structural limitations to a common genus of antibodies, and structural changes affect function in less predictable ways.”

But she emphasises that the Federal Circuit has not handed down a blanket prohibition on functional genus claims, noting that the court stated: “We do not hold that the effort required to exhaust a genus is dispositive.” The enablement requirement, says Helm: “Does not require a skilled artisan to go on and find every last antibody that falls within these claims in order to satisfy the scope of the claims analysis under *Wands*.”

This impacts innovator-versus-innovator antibody IP strategy

The decision has IP strategy implications for a commercially and technologically important area of pharma innovation. Biologics occupy an increasingly significant place in the drug market, where antibody drugs like Humira, Opdivo and Keytruda are among the best-selling prescription medicines.

Those antibody inventors with broad rights may not be able to enforce their patents. This is likely to change the dynamics of innovator-versus-innovator patent strategy, where one party seeks to exclude competitors from marketing a broad range of potential rival products (as happened in this dispute).

But it will have less impact on biosimilar disputes, thinks Helm. “Functional genus claims are not usually the issue for generic drug manufacturers, and innovators are not usually relying on functional genus claims to prevent a generic from coming on the market,” she explains. “Such claims are more frequently used to block a competitor and, from what we have seen from biosimilar litigation so far, other types of claims like manufacturing patents may be the main patents asserted against biosimilar manufacturers.”

The ruling flows from broader developments in Section 112(a) case law

While developing enablement jurisprudence, the decision does not depart from previous rulings, but extends an existing tendency in Federal Circuit opinions to find broad genus claims invalid under Section 112(a).

As *IAM* explained in a recent article, a series of appellate decisions including *ALZA v Andrx* (2010), *Wyeth & Cordis v Abbott* (2013), *Enzo v Roche* (2019) and *Idenix v Gilead* (2019) have entrenched an approach to enablement and written description that make it difficult to uphold broad genus claims in the life sciences. These cases – many of which were cited in *Amgen* – have led prominent law professors to declare the “death of the genus claim”.

For Helm, *Amgen v Sanofi* also follows a trend in which enablement is assuming greater importance to the written description requirement. “Enablement is now having its heyday,” she says. “For a long time, written description was the focal point

of 112 challenges to patents, for antibodies or otherwise. It was more common that patents would be invalidated for written description than for enablement. More recently, however, enablement has come into its own, with several recent decisions."

Amgen has suffered a dramatic reversal of fortunes

Amgen has suffered a very rapid reversal of fortunes in its cross-border PCKS9 disputes with Sanofi and Regeneron.

As recently as mid-2019, it appeared that it had the upper hand in its struggle to keep Praluent off the market. Then, the Dusseldorf Higher Regional Court held that the rival product infringed Amgen's German patents and issued an injunction. The patent owner had also fended off obviousness and insufficient disclosure oppositions to its broad rights at the EPO, as well as defending its patents in Japanese proceedings.

Things in the US were more mixed at that point, but a Delaware jury had found its patents valid and infringed in 2016, resulting in a permanent injunction. Although this decision was overturned by the Federal Circuit in 2017, Amgen had convinced another jury that its patents were valid in a 2019 retrial.

Amgen's fortunes changed after that, with the district court's August 2019 upheaval of the second jury verdict, and now with the Federal Circuit's affirmation of the lower court's decision. The EPO also invalidated key patent claims in late-2020, allowing Praluent to stay on the market.

Adam Houldsworth

Author | Life sciences reporter
adam.houldsworth@lbresearch.com

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