U.S. Federal Circuit Continues To Pressure BioPharma For More When It Comes To Functional Claims

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Biologic drugs, many of which are antibodies, represent an increasing share of the pharmaceutical market. In recent years, numerous broad functional patent claims directed at therapeutic antibodies have come under attack for failing to satisfy the written description and enablement requirements. The proper scope of these requirements has divided the biopharmaceutical industry. In its latest decision on this topic, *Amgen Inc. et al. v. Sanofi, Aventisub LLC et al.*, ___ F.3d ___, No. 2020-1074 (Fed. Cir. Feb. 11, 2021), the Federal Circuit affirmed the invalidity of claims directed to therapeutic antibodies, noting that "functional claim limitations … pose high hurdles in fulfilling the enablement requirement."

This is the second decision of the Federal Circuit in a long-running dispute between the parties. At its center are Amgen's Repatha® and Sanofi's Praluent® antibody products for the treatment of high cholesterol. Amgen first sued Sanofi and others for patent infringement in the District of Delaware in late 2014. The defendants stipulated to infringement and a jury returned a verdict in favor of Amgen, failing to find invalidity. During the first appeal, the Federal Circuit struck a significant blow to the biopharmaceutical industry by overturning the "newly characterized antigen" test, which had permitted patentees to obtain broad claims to a genus of antibodies by describing the structure of the corresponding antigen, as opposed to the antibodies themselves. The Federal Circuit also remanded the case for re-trial. Back in the district court, the jury once again found the claims valid, but the district court disagreed, issuing judgment as a matter of law that the patents lacked enablement. This second appeal followed with Bristol Myers Squibb Co., Pfizer Inc., and Eli Lilly and Company, among others, filing dueling amicus briefs.

The appealed claims cover antibodies that lower the levels of low-density lipoprotein ("LDL") cholesterol in the bloodstream. As explained by the Federal Circuit, high levels of LDL cholesterol are linked to heart disease. LDL receptors remove LDL cholesterol from the bloodstream and the receptor levels are in turn regulated by the enzyme proprotein convertase subtilisin/kexin type 9 ("PCSK9"). Antibodies that bind PCSK9 can block the degradation of the LDL receptors needed to regulate cholesterol levels. Amgen's patents claim anti-PCSK9 antibodies functionally, by reference to the locations (residues) on the PCSK9 enzyme to which the antibodies bind. A representative claim reads:

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.

The Federal Circuit decision focused on the enablement requirement, which stems from 35 U.S.C. § 112 and its purpose is to ensure an adequate quid pro quo between the patentee and the public. In exchange for a limited monopoly on the invention, the patentee must enable the public to "carry out the invention" without "undue experimentation." On appeal, however, the Federal Circuit held that the amount of experimentation needed to make and use Amgen's patent claims was too high.

In summarizing its precedents, the panel stated that "[i]n cases involving claims that state certain structural requirements and also require performance of some function (e.g., efficacy for a certain purpose), … undue experimentation can include undue experimentation in identifying, from among the many concretely identified compounds that meet the structural requirements, the compounds that satisfy the functional requirement." According to the Federal Circuit, that reasoning applied in this case as each appealed claim was a composition claim defined—not by structure—but by functional limitations, namely binding specific PCSK9 residues and blocking LDL receptor binding. The claims were, in the court's view, broad and the evidence indicated that only a small subset of the claimed antibodies could be predictably generated. To discover the many additional antibodies covered by the claims, a person of ordinary skill in the art was left to proceed "through either 'trial and error, by making changes to the disclosed antibodies and then screening those antibodies for the desired binding and blocking properties,' or else 'by discovering the antibodies *de novo*' according to a randomization-and-screening 'roadmap.'" Either way, the required experimentation "would take a substantial amount of time and effort." The Court affirmed the invalidity because the claimed "functional limitations … [were] broad, the disclosed examples and guidance [were] narrow, and no reasonable jury could conclude under these facts that anything but 'substantial time and effort' would be required to reach the full scope of claimed embodiments."

Notably, however, the Federal Circuit made clear that it may be possible to enable an entire genus, stating that it did "not hold that the effort required to exhaust a genus is dispositive." Instead, "[i]t is appropriate … to look at the amount of effort needed to obtain embodiments outside the scope of the disclosed examples and guidance." And "[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." This case thus presents a cautionary tale for patent prosecutors. Attorneys and agents must tailor functional limitations to cover only subject matter adequately disclosed by the specification either through examples or through detailed roadmaps. This is especially pertinent to practitioners in the biopharmaceutical field, which is considered an "unpredictable field of science" and, thus, faces a heightened enablement bar.