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The Tyranny of Large Numbers: Their Grip on s. 102 Inquiries

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So that I don't have to explain the claims and the arguments presented by the parties, please read my posts on the Supreme Court's opinion on Amgen v. Sanofi on May 22, 2023 and the Fed. Cir.'s opinion on February 13, 2021. In Amgen the Supreme Court affirmed the Fed. Cir.'s opinion, ruling that the disclosure of 26 antibodies did not enable the functional claims that encompassed millions of antibodies, because the effort to identify the other members of the genus would amount to undue experimentation. Earlier I wrote that "While Lourie tries to cabin the undue effort holding by writing 'We do not hold that the effort required to exhaust a genus is dispositive', he contradicts himself in the same paragraph by concluding that 'no reasonable jury could conclude under these facts that anything but 'substantial time and effort' would be required to reach the full scope of the claimer embodiments.'" The Supreme Court quoted the first sentence I quoted but ignored the second and wrote, "Instead the court stressed, the problem it saw was the same problem we see: Amgen offers persons skilled in the art little more than advice to engage in 'trial and error.'" So Sanofi succeeded in being found not-guilty of infringement of their antibody-based therapeutic simply by waiving the "at least millions of candidates" that would have to be screened for the recited bioactivity, and this effort involves "undue experimentation.

Let's step into the way-back machine to see how this sad fate of most pharma genus claims arose. In fact, we need only go far as the Fed. Cir.'s opinion in Idenix Pharm. LLC v Gilead Scis. Inc, 941 F.3d 1149 (Fed. Cir. 2019). Claim 1 is directed to purine or pyrimidine-substituted ribofuranosyl nucleosides that also have a 2?-beta-methyl substituent on the oxocyclopentyl ring. The court found that there were four working examples. While the court agreed that the synthesis and screening to locate candidates within the scope of the claims would be routine, the court found that the amount of screening necessary to support the "full scope" of the generic claims would have required "excessive experimentation" even if the synthesis and screening "tens of thousands" of compounds within the scope of the claims would have been routine. This language strongly suggests that enablement would require screening all, or at least most, of the compounds falling within the scope of the claims.

This decision and others like it led professors Karshtedt, Lemley and Seymore to publish a chilling paper entitled "The Death of the Genus Claim", Harvard Journal of Law and Technology, Vol. 35, No. 1 (Fall 2021). While they make it clear that their analysis applies only to chemical patents, like "small molecule" pharmaceuticals, they realize that it might be extended to biotech patents with claim language that is wholly functional and, of course, it has.

Picking out a section to quote is not easy, but I will try. Here is the second paragraph of page 58:

> "[I]f the PHOSITA can figure out how to make a working embodiment without too much effort — there is no reason to require more in most cases. Decisions like [Idenix], which focus on the number of species covered by the genus claim as a reason to reject it, miss the point. The genus is very large, and it would take an impossible effort to identify all the species within its scope that would work. But there's no reason anyone has to make that much effort … Anyone who wants to know if their chemical is within the scope of the claim can readily make that assessment: by hypothesis, the boundaries of a chemical genus are well-specified, and it doesn't take much effort to determine whether or not any particular chemical works for the intended purpose."

To buttress their impossible effort position the authors cite to an interesting paper by Kelly and Calvo, "Insight: The Scope of a Sextillon — How Courts Misapply Law of Enablement to Life Sciences," (May 1st, 2020). The authors demonstrate that 16 unique square paintings, placed in a 4×4 grid and each equipped with 4 possible orientations (by rotation), yield over 89 sextillion potential arrangements. "If the skilled artisan generated 1 arrangement per second, it would take 20,000 times the age of the known universe to try them all…The true measure of enablement is thus whether a skilled artisan could practice any embodiment without undue experimentation—not whether he can actually make every embodiment. The former provides the proper incentive balance to reward innovation, while the latter allows our difficulty conceptualizing very large numbers to cloud the analysis."

This misguided focus on whether or not the inventors can enable the "full scope" of the claimed invention without unreasonable experimentation—conducted by trial and error—drove the Amgen v. Sanofi decision, which, in turn recently doomed the antibody claims in Baxalta Inc. v. Genentech, Inc., no. 2022-1461 (Fed. Cir., Sept. 20, 2023). Claim 1 of U.S. Patent no. 7,033,590 reads "An isolated antibody or antibody fragment thereof that binds Factor IX or Factor IXa and increases the procoagulant activity of Factor IXa." This is a method of treatment for hemophilia. From the analysis above, you can predict that the patent was going to be held invalid as soon as the parties began analyzing the "full scope of the invention." "Baxalta argues summary judgment of invalidity was improper because, when viewing the evidence in the light most favorable to Baxalta, skilled artisans can obtain the full scope of the claimed antibodies without undue experimentation." The court simply relied on Amgen as teaching "[t]he full scope of the claims covered potentially millions of antibodies, but the specification only disclosed the amino acid sequences of 26 antibodies that performed the claimed functions." Toward the end of the opinion the court conceded that "methods like a roadmap or conservative substitution might be sufficient to enable other claims under different circumstances, such as where the patent discloses 'a quality common to every fundamental embodiment.'…In some cases, disclosing that general quality may reliably enable a person skilled in the art to make and use all that is claimed, not merely a subset."

From the discussion of big numbers above, the burden of dealing with "every fundamental embodiment" cannot be met, at least not in the known world. I am no expert in nascent technologies, but perhaps this is a job for AI. The inventors would use AI to generate useful analogs by screening properties common or related to the working examples considered as a group. For example, AI might tell us that 2', 3' substitution is more likely to have the ability to bind to the receptor than a 2', 3' double bond, after screening the first million possible analogs. AI might locate general qualities that we could never imagine, even ones that might please a future court.

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