Dosing regimen patents scrutinized by the Federal Circuit

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The validity of dosing regimen patents has recently drawn the attention of both the U.S. Court of Appeals for the Federal Circuit as well as interested pharmaceutical and chemistry groups. On Nov. 30, 2021, the Federal Circuit, in *Biogen Int'l GMBH v. Mylan Pharms. Inc*, 18 F.4th 1333 (Fed. Cir. 2021), affirmed a decision invalidating a dosage patent directed to a method of treating multiple sclerosis.

The Biogen *and* Novartis *cases highlight the scrutiny claims containing dosing limitations have drawn recently, and possible tensions within the recent Federal Circuit decisions.*

In contrast, the Federal Circuit upheld the validity of dosing regimen claims in *Novartis Pharms. Corp. v. Accord Healthcare, Inc.*, 21 F.4th 1362, 1365 (Fed. Cir. 2022). *Novartis* involved the extent to which dosages must be described in a patent's specification for patentability purposes. As discussed below, these cases highlight the scrutiny claims containing dosing limitations have drawn recently, and possible tensions within the recent Federal Circuit decisions.

The *Biogen* case involved an appeal from a district court decision invalidating U.S. Patent No. 8,399,514 (the '514 Patent), finding the claims lacked adequate written description. The '514 Patent is directed to a method for treating multiple sclerosis (MS) by providing a therapeutically effective amount of dimethyl fumarate (DMF) in the amount of "about 480 mg per day." The district court determined that the patent's specification did not show that the inventors possessed the invention on its earliest claimed priority date nor had the inventors established that a 480 mg dose of DMF "would be therapeutically effective for treating MS."

Biogen appealed to the Federal Circuit. In finding no clear error in the district court's decision, the panel majority focused on (1) the fact that the specification "casts a wide net for a myriad of neurological disorders" and (2) the fact that there was only one reference to 480 mg of DMF in the entire specification, "at the end of one range among a series of ranges." (*Biogen*, 18 F.4th at 1338, 1343).

The Court noted, "[t]he specification's sole reference to DMF480 constitutes a significant fact that cuts against Biogen's case, particularly because it appears at the end of one range among a series of ranges...." (*Id.*). The Court further noted that the specification focused exclusively on screening compounds for activation of a specific biological pathway (i.e., a focus on drug discovery), and that "the specification's focus on basic research and broad DMF-dosage ranges show that the inventors did not possess a therapeutically effective DMF480 dose at the time of filing in 2007." (*Id*. at 1343).

Biogen International BmbH and Biogen MA, Inc. filed a combined petition for panel rehearing and rehearing en banc. A response to the petition was invited by the court and filed by Mylan Pharmaceuticals Inc. The court also accepted amicus briefs filed by Biotechnology Innovation Organization, Chemistry and The Law Division of the American Chemical Society, and Pharmaceutical Research and Manufacturers of America urging the Federal Circuit to review its decision.

The three interested groups noted that Biogen's holding was inconsistent with the Court's precedent, emphasizing that "the written description requirement has never required an inventor to actually make the invention before filing a patent application[,]" "demand working examples[,]" or "that the specification itself prove the described effect."

Chemistry and the Law Division of the American Chemical Society filed a brief requesting "[c]larity in establishing what is required under 35 U.S.C. § 112 and what 'possession' of a claimed invention means." In its brief, the group noted that "[t]he panel majority's decision departs from precedent and 35 U.S.C. § 112's plain text requiring 'a written description of the invention,' and instead requires that the specification itself prove the described effect, which would require that the written description requirement mandated actual reduction to practice of the invention." Thus, if the panel's majority decision were upheld, it would "require a heightened standard for patent prosecution that conflicts with the statute and precedent."

On March 16, 2022, the Federal Circuit denied a rehearing in a precedential order without comment. *Biogen Int'l GMBH v. Mylan Pharms. Inc.*, Dkt. No. 20-1933 (Fed. Cir. 2022). While seven judges voted to let the decision for Mylan stand, three dissented from the majority noting that the ruling creates confusion about patent

eligibility. In their dissent, Circuit Judge Alan Lourie, joined by Chief Circuit Judge Kimberly Moore and Circuit Judge Pauline Newman, emphasized that the decision went against precedent that dated back to 1853. *Id*. at 6.

In contrast to *Biogen*, the Federal Circuit upheld the validity of claims of U.S. Patent No. 9,187,405 (the '405 Patent) in the *Novartis* case, finding those dosing regimen claims satisfied the written description requirement (*Novartis*, at 1365). The '405 Patent is directed to a method of treating relapsing remitting multiple sclerosis (RRMS) with a daily dose of 0.5 mg of the compound fingolimod, without an immediately preceding loading dose regimen, (hereinafter referred to as the "no-loading dose negative limitation").

The specification detailed a human prophetic trial as well as a rat EAE model. The Prophetic Trial described daily dosages of 0.5, 1.25, or 2.5 mg. '405 patent col. 11 ll. 8–16. The EAE model described a dosage of 0.3 mg/kg per week. '405 patent col. 10 ll. 64–col. 11 ll. 2.

On appeal, Defendant HEC Pharm CO. Ltd. argued that (1) there was no written description of the no-loading dose negative limitation and (2) there was also no support for the 0.5 mg daily dose limitation (*Novartis*, at 1367-1368). The Federal Circuit found the district court's validity decision was supported by substantial evidence including expert testimony.

With respect to the written description for the claimed 0.5 mg daily dose, the majority found that a skilled artisan would understand that the inventors possessed a 0.5 mg daily dose based on the 0.3 mg/kg weekly dosing regimen used in rat experiments crediting the testimony of two of Novartis' expert witnesses to make this leap.

The majority noted that the 0.5 mg daily dose was also illustrated in the prophetic human trial, and the disclosure of two other dosages did not detract from the written description of the claimed dose. With respect to the negative limitation, the majority found sufficient written description, crediting expert testimony that "[i]f a loading dose were directed, the Patent would say that a loading dose should be administered 'initially.'"

In contrast to Biogen, *the Federal Circuit upheld the validity of claims of the '405 Patent in the* Novartis *case, finding those dosing regimen claims satisfied the written description requirement.*

The *Biogen* and *Novartis* cases highlight the increasing attention and tension that dosing regimen patents have recently drawn. The three amicus briefs filed in the *Biogen* case reflect the field's interest in clarifying the written description requirement for dosage regimen patents in light of the Federal Circuit's recent decisions. Both patent challengers and owners should closely monitor the Federal Circuit's handling of dosing regimen patents in evaluating litigation strategies for challenging or maintaining the validity of such patented inventions.

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