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Recent Court Decisions

By: Chris McDonald

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Biogen Int'l v. Mylan Pharmaceuticals (Fed. Cir. 2022) (en banc denial)

Background

Mylan seeks regulatory approval for generic equivalent to Biogen's Tecfidera® (dimethyl/monomethyl fumarate) multiple sclerosis drug

US Patent 8,399,514, owned by Biogen, invalidated by Federal Circuit in December 21, 2021. Affirmed lower court's ruling for invalidity on grounds of lack of written description.

Method claim had step of administering "a therapeutically effective amount [of] about 480 mg" of DMF per day along with an excipient for treatment of multiple sclerosis

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Background

1. A method of treating a subject in need of treatment for multiple sclerosis comprising orally administering to the subject in need thereof a pharmaceutical composition consisting essentially of (a) a therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof, and (b) one or more pharmaceutically acceptable excipients, wherein the therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof is *about 480 mg per day*.

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Column 6-9

Method 1: screening for a candidate compound for treating a neurological disease comprises: a) contacting a cell with a plurality of test compounds … including compounds of Formulas I, II, III, or IV, the at least one compound is selected from fumaric acid, its salts, and fumaric acid derivatives.

Method 2: evaluating neuroprotective properties of at least one drug or drug candidate for treating at least one neurological disease … including compounds of Formulas I, II, III, or IV, the compound is fumaric acid, its salt, or a fumaric acid derivative

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Column 6-9

Method 3: methods of comparing (e.g., for bioequivalence) at least two pharmaceutical compositions… including compounds of Formulas I, II, III, or IV, the test compound is fumaric acid or its salt, or a fumaric acid derivative.

Method 4: treating a neurological disease by administering to the subject in need thereof at least one compound that is at least partially structurally similar to DMF and/or MMF… including compounds of Formulas I, II, III, or IV

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Column 6- 9

Method 5: treating a mammal having a neurological disease by combination therapy … compound of Formula I, II, III, or IV, e.g., DMF or MMF; and the at least one second compound

Column 9-11

Discussion of Formulas I, II, III, IV

Column 18 – effective amount includes "480 mg to about 720 mg per day

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Disclosure

Paneuro-degenerative diseases such as amyotrophic lateral sclerosis (ALS), Parkinson's disease, Alzheimer's disease, and Huntington's disease; demyelinating neurological diseases, such as various forms of MS and at least twenty-eight other disorders related to demyelination; polyneuritis; and mitochondrial disorders with demyelination

For example, an effective dose of DMF or MMR to be administered to a subject orally can be from about 0.1 g to 1 g per pay, 200 mg to about 800 mg per day (e.g., from about 240 mg to about 720 mg per day; or ***from about 480 mg*** to about 720 mg per day; or about 720 mg per day).

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CAFC Decision (December 2021)

Specification's only disclosure of dosage is prophetic example of "an effective dose of DMF … can be from … about 480 mg to about 720 mg per day; or about 720 mg per day."

Appellate majority noted that this was the "sole reference," the "*one and only* reference", a "single passing reference" to 480 mg/day and that it appeared "at the end of one range among a series of ranges."

The court also contrasted the 480 mg/day disclosure with the specification's disclosure of 720 mg/day that was specifically identified and elsewhere in the patent shown to be effective.

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At the time the patentee did not actually have evidence that the 480 mg/day dosage was effective.

Based on the single passing reference to a DMF480 dose in the disclosure, skilled artisan would not have recognized that DMF480 would have been efficacious in the treatment of MS, particularly because the specification's only reference to DMF480 was part of a wide DMF dosage range and not listed as an independent therapeutically efficacious dose

Post-filing research proves that 480 mg/day is effective dose

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O'Malley dissent:

Believes the majority misunderstands the differences between therapeutic and clinical efficacy and the differences between what is required to obtain a patent and what is required for FDA approval of a drug

The majority does not, and cannot, deny that the claimed DMF480 dose is expressly disclosed. To the extent the majority's opinion may be read to establish a requirement that a claim element must be disclosed multiple times, I dissent from that holding as well.

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Denial of Rehearing

Judge Lourie Dissent

1) Undue emphasis on unclaimed disclosure in the specification by comparing claimed amount to ubnnclaimed amount
2) Places burden of proof on patentee by asserting that nothing in the specification teaches one of ordinary skill that 480 mg/day is effective for MS
3) Use of case law concerning enablement in the context of operability and best mode
4) Consideration of extrinsic evidence, including Biogen's later applications

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Federal Circuit precedent does not require a patentee to show that "the specification proves the efficacy of the claimed pharmaceutical composition," citing *Nuvo Pharms. (Ir.) Designated Activity Co.*

By focusing on whether the patentee *proved* that 480 mg per day is an effective amount to treat multiple sclerosis—as distinct from whether the '514 patent specification *discloses* that 480 mg per day is an effective amount to treat multiple sclerosis—the panel majority and the district court erroneously imported operability considerations into the written description analysis

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Conclusion

Considered an outlier set of facts unlikely to arise again

Unlikely to be applied by Examiners but possibility defense to infringement

Indivior UK v. Dr. Reddy's Labs (Fed. Cir. 2022).

Federal Circuit denied an en banc petition in written description case focusing on claimed ranges

Inter partes review of US 9,687,454 found some claims anticipated by US 2011/0033541.

At issue is whether claims are entitled to filing date of earliest application; 12/537,571

Indivior UK v. Dr. Reddy's Labs

A patent cannot be directly challenged via IPR for lack of enablement or written description. However, Section 112(a) issues do arise when the challenged patent purports to claim priority back to a prior filing. The priority claim fails if the earlier filing fails to support the challenged claims, and this permits assertion of intervening prior art

Dr. Reddy challenged Invidior's U.S. Patent 9,687,454 via IPR. The '454 patent is a continuation of several applications, beginning with application No. 12/537,571, filed on Aug. 7, 2009

Indivior UK v. Dr. Reddy's Labs

Patent discloses sublingual film containing some drug treatment and claims amount of polymeric matrix used for the film.

- Claim 1: about 40 wt % to about 60 wt % of a water soluble polymeric matrix;
- Claims 7 & 12: "about 48.2 wt % to about 58.6 wt %; and
- Claim 8: "about 48.2 wt %

Indivior UK v. Dr. Reddy's Labs

Express disclosure of a claimed range can readily satisfy the written description requirement, inherent disclosure of such ranges by example is also in some cases adequate for written description purposes; *see Union Oil of Cal. v. Atl. Richfield Co.,* 208 F.3d 989, 997 (Fed. Cir. 2000)

Indivior UK v. Dr. Reddy's Labs

TABLE 1

Various Compositions of Film Dosages

Components	Buprenorphine/ Naloxone Films Unit Formula (mg per film strip) Buprenorphine/ Naloxone Ratios 16/4	12/3	8/2	2/0.5
Active Components				
Buprenorphine HCl	17.28	12.96	8.64	2.16
Naloxone HCl Dihydrate	4.88	3.66	2.44	0.61
Inactive Components				
Polyethylene Oxide, NF (MW 200,000)	27.09	20.32	13.55	—
Polyethylene Oxide, NF (MW 100,000)	12.04	9.03	6.02	19.06
Polyethylene Oxide, NF (MW 900,000)	4.82	3.62	2.41	2.05
Maltitol, NF	12.04	9.03	6.02	5.87
Flavor	6.0	4.5	3.0	2.4
Citric Acid, USP	5.92	4.44	2.96	2.96
HPMC	4.22	3.16	2.11	2.34
Ace-K	3.0	2.25	1.5	1.2
Sodium Citrate, anhydrous	2.68	2.01	1.34	1.34
Colorant	0.03	0.02	0.01	0.01
Total (mg)	100	75	50	40

TABLE 5

Formulations of Test Films at Various pH Levels

Component	Test formulation 1 8 mg/2 mg pH = 6.5 % w/w	Mg/film	Test formulation 2 8 mg/2 mg pH = 3-3.5 % w/w	Mg/film	Test formulation 3 8 mg/2 mg pH = 5-5.5 % w/w	Mg/film
Buprenorphine HCl	21.61	8.64	17.28	8.64	17.28	8.64
Naloxone HCl Dihydrate	6.10	2.44	4.88	2.44	4.88	2.44
Polymer	5.05	2.02	4.82	2.41	4.82	2.41
Polymer	28.48	11.39	27.09	13.55	27.09	13.55
Polymer	12.65	5.06	12.04	6.02	12.04	6.02
Polymer	4.43	1.77	4.22	2.11	4.22	2.11
Sweetener	12.65	5.06	12.04	6.02	12.04	6.02
Sweetener	3	1.2	3	1.5	3	1.5
Flavor	6	2.4	6	3	6	3
Citric acid	0	0	5.92	2.96	2.51	1.26
Sodium citrate	0	0	2.68	1.34	6.08	3.04
FD&C yellow #6	0.025	0.01	0.03	0.02	0.03	0.02
Total	100	40	100	50	100	50

Indivior UK v. Dr. Reddy's Labs

TABLE 2

Absorption Data for Suboxone ® products

Sample	C max	AUC
Buprenorphine (2 mg) Suboxone ® Tablet	0.780 ng/ml	6.789 hr * ng/ml
Naloxone (0.5 mg) Suboxone ® Tablet	51.30 pg/ml	128.60 hr * pg/ml
Buprenorphine (16 mg) Suboxone ® Tablet	4.51 ng/ml	44.99 hr * ng/ml
Naloxone (4 mg) Suboxone ® Tablet	259.00 pg/ml	649.60 hr * pg/ml

Indivior UK v. Dr. Reddy's Labs

One must select several components, add up the individual values, determine the aggregate percentages, and then couple those aggregate percentages with other examples in the '571 application to create an otherwise unstated range

Specification disclosed "[t]he film may contain any desired level of . . .polymer" and that in one embodiment it is "at least 25%."

Indivior UK v. Dr. Reddy's Labs

A written description sufficient to satisfy the requirement of the law requires a statement of an invention, not an invitation to go on a hunting expedition to patch together after the fact a synthetic definition of an invention

Court found that individual point of "about 48.2 wt %" was supported by the original specification "given that claim 8 does not recite a range, but only a specific amount, which can be derived by selection and addition of the amounts of selected"

Indivior UK v. Dr. Reddy's Labs

Specification described several embodiments covered by the claims, it did not describe the full-scope of the claimed invention

Questions?

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