IN THE
SUPREME COURT OF THE UNITED STATES

No. _____

NOVARTIS PHARMACEUTICALS CORPORATION,

v.

HEC PHARM CO., LTD., HEC PHARM USA INC.

APPLICATION FOR AN EXTENSION OF TIME WITHIN WHICH TO FILE A PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

THOMAS G. HUNGAR
JACOB T. SPENCER
GIBSON, DUNN & CRUTCHER LLP
1050 Connecticut Avenue, NW
Washington, DC 20036
Tel: (202) 955-8500

JANE M. LOVE, PH.D.
ROBERT TRENCHARD
GIBSON, DUNN & CRUTCHER LLP
200 Park Avenue
New York, NY 10166
Tel.: (212) 351-4000

DEANNE MAYNARD
Counsel of Record
SETH W. LLOYD
MORRISON & FOERSTER LLP
2100 L Street, NW, Suite 900
Washington, DC 20037
Tel.: (202) 887-1500
DMaynard@mofo.com

WILLIAM M. JAY
GOODWIN PROCTER LLP
1900 N Street, NW
Washington, DC 20036
Tel: (202) 346-4000

DAVID ZIMMER
EDWINA CLARKE
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
Tel: (617) 570-1000

Counsel for Novartis Pharmaceuticals Corporation

December 6, 2022

RULE 29.6 STATEMENT

Novartis is a wholly owned subsidiary of Novartis AG, and no other publicly traded company owns 10% or more of its stock. *See* S. Ct. R. 29.6.

PARTIES TO THE PROCEEDING

All parties to the case in the court of appeals appear in the caption of this application. Various other companies were defendants in the district court but were not parties to the appeal.

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NOVARTIS PHARMACEUTICALS CORPORATION,

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HEC PHARM CO., LTD., HEC PHARM USA INC.

APPLICATION FOR AN EXTENSION OF TIME WITHIN WHICH TO FILE A PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

To the Honorable John G. Roberts, Jr., Chief Justice of the Supreme Court of the United States:

Applicant Novartis Pharmaceuticals Corporation ("Novartis") requests a 30-day extension from December 19, 2022, to and including January 18, 2023, within which to file a petition for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit in this case.

The Federal Circuit initially entered judgment on January 3, 2022. App., *infra*, 27a-56a. After HEC Pharm Co., Ltd. and HEC Pharm USA Inc. (collectively "HEC") filed a combined petition for panel and/or en banc rehearing, a differently composed Federal Circuit panel vacated the original judgment and entered a new judgment on June 21, 2022. App., *infra*, 1a-15a. Novartis filed a combined petition for panel and/or en banc rehearing on July 21, 2022, which the Federal Circuit denied on

September 20, 2022. App., *infra*, 115a-117a. A petition for a writ of certiorari is currently due on December 19, 2022. This application is being filed more than ten days before that date. *See* S. Ct. R. 13.5.

The jurisdiction of this Court would be invoked under 28 U.S.C. § 1254(1). Copies of the opinions of the court of appeals, the order denying rehearing and rehearing en banc, and the district court opinion are attached to this application. App., *infra*, 1a-117a.

1. This is a patent case in which four Federal Circuit judges evenly divided on the correct interpretation of the patent law that should apply to Novartis's patent. The case stems from HEC's undisputed infringement of a Novartis patent. App., *infra*, 4a. Novartis invented and patented a new method for treating a specific type of multiple sclerosis with a lower drug dose than previously thought necessary. App., *infra*, 3a-4a. Novartis markets the lower dose of the drug under the brand name Gilenya. Gilenya was a breakthrough—the first-ever oral medication for treating a certain type of multiple sclerosis. App., *infra*, 3a.

As contemplated by the Hatch-Waxman Act governing patent disputes over generic drugs, Novartis asserted its patent against more than 20 companies that sought FDA approval to market generic versions of Gilenya in an infringing manner. App., *infra*, 4a. After the district court granted Novartis a preliminary injunction, every defendant but HEC settled. At a bench trial, HEC attempted to prove by clear and convincing evidence that Novartis's patent was invalid because it failed to describe the claimed invention adequately. After hearing live testimony from six

expert witnesses and deposition testimony from several fact witnesses, the trial court issued a detailed decision rejecting HEC's invalidity challenge on the facts. App., *infra*, 71a-114a. Among other things, the trial court credited Novartis's expert testimony about how persons of ordinary skill in this complex medical field would understand the patent's description of animal testing and a prophetic clinical trial. App., *infra*, 94a-99a. The court also noted that HEC left key evidence unrebutted—indeed, HEC's expert conceded he was unqualified to opine on the meaning of critical parts of Novartis's patent because he lacked relevant technical experience. App., *infra*, 94a-99a.

2. On HEC's appeal, the Federal Circuit initially affirmed the judgment, with Chief Judge Moore dissenting. In a precedential decision, the initial panel majority (Judges O'Malley and Linn) rejected HEC's attempt to impose a "heightened" standard for a patent to describe an invention adequately. App., *infra*, 27a-56a. The panel emphasized instead that the "description requirement is essentially a fact-based inquiry" because "it is how a skilled artisan reads a disclosure that matters." App., *infra*, 47-48a. On that fact-based inquiry, the panel found ample evidence to support the district court's "quite carefully" conducted "'objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill.'" App., *infra*, 49a. The panel thus affirmed the district court's no-invalidity finding and entered judgment for Novartis. App., *infra*, 42a-56a.

3. The Federal Circuit subsequently reversed itself, solely because of a change in the panel's membership. After HEC filed its rehearing petition and

Novartis filed an expedited response, the original decision's author, Judge O'Malley, retired from the court. Three months later, a panel of Chief Judge Moore (originally in dissent), Judge Linn (originally in the majority), and Judge Hughes (not on the original panel) purported to grant "panel" rehearing, vacated the prior precedential opinion, and entered a new, divided precedential decision reversing the district court.

The new opinion identified no basis for granting rehearing—for example, a point of law or fact that the original panel "overlooked or misapprehended," Fed R. App. P. 40(a)(2). It never noted the change in panel membership. Instead, the new panel simply entered a new decision that was, in substance, the original dissent recast as a majority. The new majority decision embraced the legal standard that the original majority had rejected as an improper heightened burden. App., *infra*, 5a-8a. Under that standard, the new decision refused to defer to the district court's factual findings about how a skilled artisan would have understood the patent's technical description of the invention. App., *infra*, 8a-14a. The new majority held that the appellate court could disregard findings and expert testimony that were "inconsistent with" how the court read "the plain text" of the patent or "at odds with" how the court read statements made during prosecution of the patent. App., *infra*, 9a, 12a.

Judge Linn, who had formed the original majority with now-retired Judge O'Malley, dissented. He adhered to the original majority opinion's reasoning and criticized the new majority decision's "heightened written description standard." App., *infra*, 16a-26a.

4. Novartis, supported by multiple amici, filed a petition for panel and en banc rehearing on two grounds—(1) in substituting a new judge to reverse the original precedential panel decision, the Federal Circuit violated statutory requirements and joined the minority side of a split among the courts of appeals; and (2) by applying a new heightened burden for a patent's description and disregarding trial court factfinding, the Federal Circuit contravened statutory text in a manner that conflicted with this Court's precedent and the Federal Circuit's own precedent. Novartis Rehearing Pet'n 7-17; *see Teva Pharms. USA v. Sandoz, Inc.*, 574 U.S. 318, 330-31 (2015) (rejecting a special patent-law exception to rule that appellate courts must defer to trial court conclusions on factual questions). The court of appeals denied rehearing. App., *infra*, 115a-117a. The Federal Circuit and this Court denied Novartis's request to stay the mandate pending the filing and disposition of a petition for a writ of certiorari.

5. Novartis requests a 30-day extension of time within which to file a petition for a writ of certiorari seeking review of the Federal Circuit's decision. Good cause exists for granting the request. A 30-day extension would allow counsel of record—who entered an appearance only at the rehearing stage in the Federal Circuit—sufficient time to review the extensive record, research and analyze the issues presented, and prepare the petition for filing.

Counsel also had and have a number of other pending matters that will interfere with counsel's ability to file the petition on December 19, 2022. Counsel recently filed an opening brief on November 7 in *Johnson v. McDonough*, No. 22-1883

(Fed. Cir.); a reply brief on November 15 in *Teradata Corporation v. SAP SE*, No. 22-1286 (Fed. Cir.); and a petition for rehearing on November 30 in *In re Monolithic Power Systems*, No. 22-153 (Fed. Cir.). Counsel also currently have an opening brief due January 6 in *ams Sensors USA Inc. v. Renesas Electronics America, Inc.*, Nos. 22-2185, 22-2186 (Fed. Cir.); a reply brief due January 9 in *Johnson v. McDonough*, No. 22-1883 (Fed. Cir.); and a response brief due January 17 in *Lynwood Investments CY Limited v. Maxim Konovalov*, No. 22-16399 (9th Cir.).

CONCLUSION

For these reasons, Novartis requests that the Court extend the time within which to file a petition for a writ of certiorari in this matter to and including January 19, 2023.

Dated: December 6, 2022

Respectfully submitted,

DEANNE E. MAYNARD
Counsel of Record
SETH W. LLOYD
MORRISON & FOERSTER LLP
2000 Pennsylvania Avenue NW
Washington, DC 20006
DMaynard@mofo.com
Tel.: (202) 887-8740

JANE M. LOVE, PH.D.
ROBERT TRENCHARD
GIBSON, DUNN & CRUTCHER LLP
200 Park Avenue
New York, NY 10166
Tel.: (212) 351-4000

THOMAS G. HUNGAR
JACOB T. SPENCER
GIBSON, DUNN & CRUTCHER LLP
1050 Connecticut Avenue, NW
Washington, DC 20036
Tel: (202) 955-8500

WILLIAM M. JAY
GOODWIN PROCTER LLP
1900 N Street, NW
Washington, DC 20036
Tel: (202) 346-4000

DAVID ZIMMER
EDWINA B. CLARKE
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
Tel: (617) 570-1000

Counsel for Novartis Pharmaceuticals Corporation

No. _____

NOVARTIS PHARMACEUTICALS,

V.

ACCORD HEALTHCARE, INC.

CERTIFICATE OF SERVICE

I, Deanne E. Maynard, hereby certify that I am a member of the Bar of this Court, and that I have this 6th day of December, 2022, caused one copy of the Application For An Extension of Time Within Which To File A Petition For A Writ of Certiorari to the United States Court of Appeals for the Federal Circuit to be served on the following counsel by third-party carrier and also by electronic mail.

Mieke K. Malmberg
SKIERMONT DERBY LLP
633 West 5th Street, Suite 5800
Los Angeles, CA 90071
mmalmberg@skiermontderby.com

Peter K. Stris
Stris andMaher llp
777 S. Figueroa Street
Suite 3850
Los Angeles, CA 90017
pstris@stris.com

Paul Skiermont
Sarah Elizabeth Spires
SKIERMONT DERBY LLP
1601 Elm Street, Suite 4400
Dallas, TX 75201
pskiermont@skiermontderby.com
sspires@skiermontderby.com

Dated: December 6, 2022

Deanne Maynard

Appendix

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APPENDIX A

United States Court of Appeals for the Federal Circuit

NOVARTIS PHARMACEUTICALS CORPORATION,
Plaintiff-Appellee

v.

ACCORD HEALTHCARE, INC., AUROBINDO PHARMA LTD., AUROBINDO PHARMA USA, INC., DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., EMCURE PHARMACEUTICALS LTD., HERITAGE PHARMACEUTICALS INC., GLENMARK PHARMACEUTICALS INC., USA, GLENMARK PHARMACEUTICALS LIMITED, HETERO USA, INC., HETERO LABS LIMITED UNIT-V, HETERO LABS LIMITED, MYLAN PHARMACEUTICALS, INC., PRINSTON PHARMACEUTICAL INC., STRIDES GLOBAL PHARMA PRIVATE LIMITED, STRIDES PHARMA, INC., TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD., ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., APOTEX INC., APOTEX CORP., SUN PHARMACEUTICAL INDUSTRIES, LTD., SUN PHARMACEUTICAL INDUSTRIES INC., SUN PHARMA GLOBAL FZE,
Defendants

HEC PHARM CO., LTD., HEC PHARM USA INC.,
Defendants-Appellants

2021-1070

Appeal from the United States District Court for the District of Delaware in No. 1:18-cv-01043-KAJ, Circuit Judge Kent A. Jordan.

Decided: June 21, 2022

JANE M. LOVE, Gibson, Dunn & Crutcher LLP, New York, NY, argued for plaintiff-appellee. Also represented by PAUL E. TORCHIA, ROBERT TRENCHARD.

PAUL SKIERMONT, Skiermont Derby LLP, Dallas, TX, argued for defendants-appellants. Also represented by SARAH ELIZABETH SPIRES; MIEKE K. MALMBERG, Los Angeles, CA.

Before MOORE, *Chief Judge*, LINN and HUGHES, *Circuit Judges*.

Opinion for the court filed by *Chief Judge* MOORE.

Dissenting opinion filed by *Circuit Judge* LINN.

MOORE, *Chief Judge*.

HEC Pharm Co., Ltd. and HEC Pharm USA Inc. (collectively, HEC) petition for rehearing of our prior decision in this case, 21 F.4th 1362 (Fed. Cir. 2022), in which we affirmed a final judgment of the United States District Court for the District of Delaware. The district court determined that claims 1–6 of U.S. Patent No. 9,187,405 are not invalid and that HEC infringes them. Because the '405 patent fails to disclose

the absence of a loading dose, the district court clearly erred in finding that the negative claim limitation "absent an immediately preceding loading dose" added during prosecution to overcome prior art satisfies the written description requirement of 35 U.S.C. § 112(a). We grant HEC's petition for panel rehearing, vacate our prior decision, and reverse the district court's judgment that Novartis' claims are not invalid for inadequate written description.

BACKGROUND

The '405 patent discloses methods of treating relapsing-remitting multiple sclerosis (RRMS) using the immunosuppressant fingolimod. *E.g.*, '405 patent at claim 1, 8:56–60. Each claim of the '405 patent requires administering fingolimod "at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen." *Id.* at claim 1. A loading dose is a "higher-than-daily dose . . . usually given as the first dose." J.A. 27 ¶ 63 (internal quotation marks omitted). The patent's specification does not mention loading doses, much less the absence of a loading dose. Instead, it describes administering fingolimod at regular intervals (e.g., once daily, multiple times per day, or every other day). '405 patent at 11:20–38.

Novartis owns the '405 patent and markets a drug under the brand name Gilenya that purportedly practices the patent. HEC filed an abbreviated new drug application (ANDA) with the Food and Drug Administration seeking approval to market a generic version

of Gilenya. Novartis sued HEC in the District of Delaware, alleging that HEC's ANDA infringes all claims of the '405 patent.[1]

After a four-day bench trial, the district court found that HEC's ANDA infringes and that the claims are not invalid, either as anticipated by Kappos 2006 or for inadequate written description of the no-loading-dose or daily-dosage limitations. HEC appeals as to written description. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

"Whether a claim satisfies the written description requirement is a question of fact that, on appeal from a bench trial, we review for clear error." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1308 (Fed. Cir. 2015) (quoting *Alcon Rsch. Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014)). Under the clear error standard, we defer to the district court's findings "in the absence of a definite and firm conviction that a mistake has been made." *Scanner Techs. Corp. v. ICOS Vision Sys. Corp. N.V.*, 528 F.3d 1365, 1374 (Fed. Cir. 2008) (cleaned up). Inadequate written description must be shown by clear and convincing evidence. *Hynix Semiconductor Inc. v. Rambus Inc.*, 645 F.3d 1336, 1351 (Fed. Cir. 2011) (citing *ICU Med., Inc. v. Alaris Med. Sys., Inc.*, 558 F.3d 1368, 1376 (Fed. Cir. 2009)).

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[1] Novartis sued several other defendants who also filed ANDAs, but those cases were settled or stayed before trial.

A

To satisfy the written description requirement, a patent's specification must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). Such possession must be "shown in the disclosure." *Id.* It is not enough that a claimed invention is "an obvious variant of that which is disclosed in the specification." *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). Disclosure is essential; it is "the *quid pro quo* of the right to exclude." *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 484 (1974); *see also Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 970 (Fed. Cir. 2002) ("[D]escription is the *quid pro quo* of the patent system.").

For negative claim limitations, like the no-loading-dose limitation at issue here, there is adequate written description when, for example, "the specification describes a reason to exclude the relevant [element]." *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1351 (Fed. Cir. 2012); *Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1355 (Fed. Cir. 2015) (same); *Nike, Inc. v. Adidas AG*, 812 F.3d 1326, 1348 (Fed. Cir. 2016) (same), *overruled on other grounds by Aqua Prods., Inc. v. Matal*, 872 F.3d 1290, 1301 (Fed. Cir. 2017) (en banc). A reason to exclude an element could be found in "statements in the specification expressly listing the disadvantages of using" that element. *Santarus*, 694 F.3d at 1351. Another reason could be that the

specification "distinguishes among" the element and alternatives to it. *Inphi*, 805 F.3d at 1357; *see also In re Johnson*, 558 F.2d 1008, 1017–19 (C.C.P.A. 1977) (reversing rejection for inadequate written description where specification disclosed several species of a genus and claims recited genus but excluded two species of lost interference count).

The common denominator of these examples is disclosure of the element. That makes sense because "the hallmark of written description is disclosure." *Ariad*, 598 F.3d at 1351; *see also Lockwood*, 107 F.3d at 1571 ("It is the disclosures of the applications that count."). Silence is generally not disclosure. *See Seabed Geosolutions (US) Inc. v. Magseis FF LLC*, 8 F.4th 1285, 1288 (Fed. Cir. 2021) ("[S]ilence does not support reading the claims to exclude gimbaled geophones." (citations omitted)); MPEP § 2173.05(i) (9th ed. Rev. 10.2019, June 2020) ("The mere absence of a positive recitation is not a basis for an exclusion."). If it were, then every later-added negative limitation would be supported so long as the patent makes no mention of it. While a negative limitation need not be recited in the specification *in haec verba*, there generally must be something in the specification that conveys to a skilled artisan that the inventor intended the exclusion, such as a discussion of disadvantages or alternatives. Consistent with our precedent in *Santarus, Inphi* and *Nike*, the written description requirement cannot be met through simple disregard of the presence or absence of a limitation.

While a written description's silence about a negative claim limitation is a useful and important clue and may often be dispositive, it is possible that the written description requirement may be satisfied when a skilled artisan would understand the specification as inherently disclosing the negative limitation.[2] For example, if the record established that in a particular field, the absence of mention of a limitation necessarily excluded that limitation, written description could be satisfied despite the specification's silence. *See Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1159 (Fed. Cir. 1998) ("[M]issing descriptive matter must necessarily be present in the . . . specification such that one skilled in the art would recognize such a disclosure." (citing *Cont'l Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991))); *see also In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) ("To establish inherency [for purposes of anticipation], . . . evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill."

---

[2] Novartis contends the written description requirement may be satisfied by "implicit disclosure" as distinct from express or inherent disclosure. Novartis Br. 50–51. Yet it fails to identify any case holding that "implicit disclosure" (whatever that means) is sufficient. Novartis cites *In re Kolstad*, a non-precedential decision involving *express* disclosure. 907 F.2d 157 (Fed. Cir. 1990) (non-precedential). If an implicit disclosure is one that would render the limitation obvious to a skilled artisan, such a disclosure cannot under our precedent satisfy the written description requirement. *Lockwood*, 107 F.3d at 1572 ("A description which renders obvious the invention for which an earlier filing date is sought is not sufficient.").

(internal quotation marks and citation omitted)). When the specification is itself silent regarding a negative limitation, testimony from a skilled artisan as to possibilities or probabilities that the recited element would be excluded would not suffice, lest such testimony could effectively eliminate the written description requirement. If silence were generally sufficient, all negative limitations would be supported by a silent specification. If, however, a patent owner could establish that a particular limitation would always be understood by skilled artisans as being necessarily excluded from a particular claimed method or apparatus if that limitation is not mentioned, the written description requirement would be satisfied despite the specification's silence.

B

The district court found that because there is no recitation of a loading dose in the specification, the no-loading-dose limitation is supported. J.A. 26 ¶ 61. The district court further found that the no-loading-dose limitation is disclosed in the specification because "[t]he Prophetic Trial describes giving a 'daily dosage of 0.5 . . . mg' fingolimod to treat RRMS, started 'initially.' The Prophetic Trial tells a person of skill that on day 1, treatment begins with a daily dose of 0.5 mg, not a loading dose." J.A. 26 ¶ 62 (citations omitted). Novartis, likewise, argues that the specification satisfies the written description requirement for the no-loading-dose limitation because it indicates that the dosing

regimen starts by "initially" administering a daily dosage. Novartis Br. 44.

The district court's finding that the specification discloses "initially" starting with a daily dose was clearly erroneous. The specification nowhere describes "initially" administering a daily dosage. The specification says, "Initially patients receive treatment for 2 to 6 months." '405 patent at 11:13–14. This sentence speaks to the initial length of treatment, not the dosage with which treatment begins. Dr. Lublin, one of Novartis' physician experts, admitted this:

> Q. And then . . . there's a sentence that begins: Initially, patients receive treatment for two to six months. Do you see that?
>
> A. I do.
>
> Q. And what does that tell you about how the dosing would work?
>
> A. It suggests to me they're taking the dosing that's outlined in that first sentence *continually for two to six months.*

J.A. 22792 (emphasis added).

The contrary testimony of Novartis' second physician expert, Dr. Steinman, is inconsistent with the plain text of the specification and therefore carries no weight. J.A. 23343 (testifying that "initially" is "really zooming in on Day 1" and conveying that treatment starts with "a daily dose of 0.5"). "[E]xpert testimony that is inconsistent with unambiguous intrinsic evidence should be accorded no weight." *Bell & Howell*

Document Mgmt. Prods. Co. v. Altek Sys., 132 F.3d 701, 706 (Fed. Cir. 1997) (citations omitted). As HEC argues in its rehearing petition, the district court's reliance on a misquotation "ferreted into trial testimony by Novartis' experts" was clearly erroneous. Pet. for Reh'g 6; *see* J.A. 26–27 ¶¶ 62–63 (district court relying on testimony that specification describes "initially" administering daily dosage).

The '405 specification discloses neither the presence nor absence of a loading dose. Loading doses—whether to be used or not—are simply not discussed. Novartis' experts readily admitted this. J.A. 23344 ("Q. Is there anywhere in [the specification] that you saw reference to the loading dose? A. No."); J.A. 22791 (Dr. Lublin testifying that "information of having a loading dose is not there"). Dr. Lublin also agreed that "[n]othing in the text of the specification of the '405 patent discloses a rationale for the negative limitation prohibiting an immediately preceding loading dose." J.A. 22872–73. The fact that the specification is silent about loading doses does not support a later-added claim limitation that precludes loading doses.

The district court also found, independent of the misquoted "initially" language, that the specification's disclosure of a daily dosage combined with its silence regarding a loading dose would "tell a person of skill that loading doses are excluded from the invention."

J.A. 26 ¶ 61. That, too, was clearly erroneous. Novartis does not defend this finding.[3] And for good reason.

There is significant tension in the district court's finding that the specification's disclosure excludes a loading dose, but that the Kappos 2006 abstract does not. Both are silent regarding loadings doses, and both disclose a daily dosage. The district court defended this inconsistency by claiming that "[u]nlike a patent, which is presumed complete, an abstract [like Kappos 2006] is not presumed to contain all of the necessary information about the study." J.A. 30 ¶ 74. This concept that a patent is presumed "complete" infected the district court's analysis and the experts' testimony regarding the no-loading-dose limitation. For example, Dr Lublin testified:

> Q. What would a person of skill reading the patent have thought about [the] question [of written description]?
>
> A. They would have viewed the patent as a document, as a complete document, that should give you all the information you need to carry out the claims, and that information of having a loading dose is not there, and what's instead there is examples of daily dose, daily dose, daily dose.

J.A. 22791. A patent is not presumed complete such that things not mentioned are necessarily excluded.

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[3] Nor could it. Novartis admittedly did not "argue below that inherency . . . applies to the '405 Patent's method claims." Novartis Br. 50. Any defense of the district court's finding is thus forfeit.

We presume only that a patent has adequate written description, not that it is complete. *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195 (Fed. Cir. 1999) ("The presumption of validity includes a presumption that the patent complies with § 112." (citing *N. Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990))).

Importantly, the disclosure of a daily dosage cannot amount to a disclosure that there can be no loading dose, because such a finding is at odds with the prosecution history. The Patent Office allowed the claims only after the applicants added the no-loading-dose limitation. J.A. 23903 (examiner's rejection in parent application); J.A. 23892–93 (applicants' response); *see also* Novartis Br. 11–12. The applicants explained that they added the no-loading-dose limitation "to specify that the [daily dosage] cannot immediately follow a loading dose regimen" and "to further distinguish their claims from the disclosure of [prior art]." J.A. 23892. If reciting "daily dosage" without mentioning a loading dose necessarily excluded a loading dose, there would have been no reason for the applicants to add the no-loading-dose limitation. Neither the applicants nor the examiner understood the words "daily dosage" without the words "no loading dose" to convey the absence of a loading dose. Accordingly, the district court's contrary finding was clearly erroneous.

There is expert testimony that the specification discloses the absence of a loading dose. Dr. Steinman testified:

> Q. And do you see the sentence there, it says, "Initially patients receive treatment for 2 to 6 months." What would that tell a person of skill?
>
> A. Well, there were two places [in the specification] that if there were going to be an immediately preceding loading dose, you would give it before the initial treatment, so you would really necessarily want to put it right there. And the second place was earlier when you talked about a daily dosage of 0.5. But there were two gates that if you wanted to interject something about a loading dose, those were the opportunities in this. And it was zero out of two places where they, I think, necessarily would have put it in.

J.A. 23334–35. This expert testimony is focused on where in the specification the patentee would have mentioned a loading dose if they intended a loading dose to be included. But the question is not whether the patentee intended there to be a loading dose; the question is whether the patentee precluded the use of a loading dose. On this record, there is no evidence that a skilled artisan would understand silence regarding a loading dose to *necessarily exclude* a loading dose. In fact, all the experts agreed that loading doses are sometimes given to MS patients. *See* J.A. 22780 (Dr. Lublin explaining that loading doses have been used in trials of MS drugs and with fingolimod in particular); J.A. 22794; J.A. 23347–48 (Dr. Steinman acknowledging that loading doses are used in MS treatments); J.A. 23475 (Dr. Jusko, Novartis' pharmacology expert,

testifying that fingolimod was given to transplant patients with a loading dose, and that he "could envision the possibility of starting with a loading dose"). And, importantly, there is intrinsic evidence that a skilled artisan would not understand reciting a daily dosage regimen without mentioning a loading dose to exclude a loading dose.

We do not today create a heightened standard for negative claim limitations. Just as disclosure is the "hallmark of written description" for positive limitations, *Ariad*, 598 F.3d at 1351, so too for negative limitations. That disclosure "need not rise to the level of disclaimer." *Santarus*, 694 F.3d at 1351. Nor must it use the same words as the claims. *Lockwood*, 107 F.3d at 1572 ("[T]he exact terms need not be used *in haec verba*." (citing *Eiselstein v. Frank*, 52 F.3d 1035, 1038 (Fed. Cir. 1995))). Rather, as with positive limitations, the disclosure must only "reasonably convey[ ] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad*, 598 F.3d at 1351. While silence will not generally suffice to support a negative claim limitation, there may be circumstances in which it can be established that a skilled artisan would understand a negative limitation to necessarily be present in a disclosure. This is not such a case.

CONCLUSION

The district court's finding that the no-loading-dose limitation meets the written description

requirement was clearly erroneous. We grant HEC's petition for panel rehearing, vacate our prior decision, and reverse the district court's judgment that the claims of the '405 patent are not invalid. We need not reach HEC's argument that the district court also clearly erred in finding adequate written description for the "daily dosage of 0.5 mg" limitation.

REVERSED

COSTS

No costs.

United States Court of Appeals
for the Federal Circuit

NOVARTIS PHARMACEUTICALS CORPORATION,
Plaintiff-Appellee

v.

ACCORD HEALTHCARE, INC., AUROBINDO PHARMA LTD., AUROBINDO PHARMA USA, INC., DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., EMCURE PHARMACEUTICALS LTD., HERITAGE PHARMACEUTICALS INC., GLENMARK PHARMACEUTICALS INC., USA, GLENMARK PHARMACEUTICALS LIMITED, HETERO USA, INC., HETERO LABS LIMITED UNIT-V, HETERO LABS LIMITED, MYLAN PHARMACEUTICALS, INC., PRINSTON PHARMACEUTICAL INC., STRIDES GLOBAL PHARMA PRIVATE LIMITED, STRIDES

PHARMA, INC., TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD., ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., APOTEX INC., APOTEX CORP., SUN PHARMACEUTICAL INDUSTRIES, LTD., SUN PHARMACEUTICAL INDUSTRIES INC., SUN PHARMA GLOBAL FZE,
Defendants

HEC PHARM CO., LTD., HEC PHARM USA INC.,
Defendants-Appellants

2021-1070

Appeal from the United States District Court for the District of Delaware in No. 1:18-cv-01043-KAJ, Circuit Judge Kent A. Jordan.

LINN, *Circuit Judge*, dissenting.

The majority, while recognizing that written description support is a fact-based inquiry based on the understandings of a person of ordinary skill in the art, and while ultimately recognizing that the standard for negative limitations is the same as for any other limitation, nonetheless applies a heightened written description standard to the facts of this case in requiring not only a "reason to exclude" but a showing that the negative limitation in question was "necessarily excluded." In doing so, the majority characterizes the district court's fact finding as clearly erroneous and concludes that written description support for the

no-load limitation is lacking. In my opinion, the district court applied the correct standard and found ample support in the written description for the no-load limitation. For these reasons, I respectfully dissent.

I

A specification that "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date" has adequate written description of the claimed invention. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.* Our case law makes clear that "[c]ompliance with the written description requirement is essentially a fact-based inquiry that will 'necessarily vary depending on the nature of the invention claimed.'" *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 963 (Fed. Cir. 2002) (quoting *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1562 (Fed. Cir. 1991)). It is well established that there is no "new and heightened standard for negative claim limitations." *Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1356 (Fed. Cir. 2015). While the court in *Santarus, Inc. v. Par Pharmaceutical, Inc.* observed that "[n]egative claim limitations are adequately supported when the specification describes a reason to exclude the relevant limitation," we did not hold that a specification *must* describe a reason to exclude a negative limitation. 694 F.3d 1344, 1351 (Fed. Cir. 2012). A specification that describes a reason to

exclude the relevant negative limitation is but one way in which the written description requirement may be met.

The majority begins its opinion with the recognition that a written description's silence about a negative claim limitation, while serving as a "useful and important clue," is not necessarily dispositive of whether that limitation is adequately supported. Maj. at 6. I agree. The majority concludes with a citation to *Ariad* for the proposition that "as with positive limitations, the disclosure must only 'reasonably convey [] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.' " Maj. at 12 (citing *Ariad*, 598 F.3d at 1351). With that, I also agree. But the majority in its analysis employs the heightened standard of "necessary exclusion" against which to assess the district court's fact findings in this case and uses that standard to conclude that the district court clearly erred. With that, I cannot agree. While a showing of "necessary exclusion" would most certainly provide written description support for a negative limitation, it is not and should not be a requirement in every case. As noted above and as *Ariad* makes clear, the critical question in assessing written description support for a negative limitation is the same as for any other limitation: "Does the written description reasonably convey to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date?" *See Ariad*, 598 F.3d at 1351. How that question is resolved depends on the

facts of each case, assessed through the eyes of the skilled artisan. Our precedent makes that clear.

For example, in *Santarus*, we found that claims directed to a method of treatment with a pharmaceutical composition containing no sucralfate were adequately described by a specification that explained that, although sucralfate is "possibly the ideal agent for stress ulcer prophylaxis," it was known to have occasional adverse effects. 694 F.3d 1344, 1350–51 (Fed. Cir. 2012). In *Santarus*, as in this case, there was expert testimony providing a person of ordinary skill's understanding of the patent specification. *See id.* at 1351. The expert testimony in *Santarus* showed that "a person of ordinary skill in this field . . . would have understood from the specification that disadvantages of sucralfate may be avoided by the [claimed] formulation." *Id.*

In *In re Bimeda Research & Development Ltd.*, we held that a claim that excluded a specific anti-infective, acriflavine, was not adequately described by a disclosure that was inconsistent with the exclusion of acriflavine but not other anti-infectives or antibiotics. 724 F.3d 1320, 1324 (Fed. Cir. 2013). The claim at issue in *Bimeda* was directed to a method of preventing mastitis in dairy cows by sealing the teat canal of a cow's mammary gland with a seal formulation that excludes acriflavine. Other claims in the same patent excluded all anti-infective agents. We noted that the patent repeatedly distinguished the invention as able to prevent mastitis without the use of antibiotics. Based on the written description's consistent description of the

invention's non-antibiotic approach to preventing mastitis, we concluded that the patent's disclosure was "inconsistent with a claim which excludes acriflavine, but *not* the presence of other anti-infectives or antibiotics." *Id.* (citation and quotation marks omitted). We did not require that the specification describe a reason to exclude acriflavine specifically; rather, we found only that a negative limitation which is inconsistent with the disclosure is not adequately described.

In *Inphi*, we confirmed that the written description requirement is satisfied where " 'the essence of the original disclosure' conveys the necessary information—'regardless of *how* it' conveys such information, and regardless of whether the disclosure's 'words [a]re open to different interpretation[s].' " 805 F.3d at 1354 (quoting *In re Wright*, 866 F.2d 422, 424–25 (Fed. Cir. 1989) (citation and internal quotation marks omitted, emphasis in *Inphi*)). We explained that "*Santarus* simply reflects the fact that the specification need only satisfy the requirements of § 112, paragraph 1 as described in this court's existing jurisprudence." *Id.* at 1356. And we noted that the " 'reason' required by *Santarus* is provided, for instance, by properly describing alternative features of the patented invention." *Id.* (citing *In re Johnson*, 558 F.2d 1008, 1019 (C.C.P.A. 1977)).

In *Inphi*, we found that substantial evidence supported the Patent Trial and Appeal Board's ("Board") finding that a negative limitation which had been added during prosecution ("DDR chip selects that are not CAS, RAS, or bank address signals") was

adequately described by an original specification which did not expressly articulate a reason to exclude RAS and CAS signals. We found the Board's decision was supported by evidence of (1) standards set by the Joint Electron Device Engineering Council, a global standard-setting body for the microelectronics industry, incorporated by reference in the patent, which specify that DDR signals, including CAS, RAS, CAS, and bank address signals, are distinct from each other; (2) a table in the specification which excludes RAS and CAS signals; and (3) various passages from the specification, including a figure which distinguishes chip select signals, command signals (including RAS and CAS signals) and bank address signals. We concluded that the specification's disclosure of alternative features was sufficient to satisfy the written description standard for the negative limitation. *Id.* at 1357.

In *Nike, Inc. v. Adidas AG*, we reiterated that *Santarus* did not create a heightened standard for written description of negative limitations. 812 F.3d 1326, 1348 (Fed. Cir. 2016), *overruled on other grounds by Aqua Prods., Inc. v. Matal*, 872 F.3d 1290 (Fed. Cir. 2017) (en banc). We stated that negative limitations, like all other limitations, are held to "the customary standard for the written description requirement." *Id.* In *Nike*, we found a limitation of "flat knit edges," which Adidas characterized as a negative limitation, was adequately described by three figures in the specification depicting the claimed textile element which Nike's expert opined could be made using flat knitting in contrast to another figure's textile element which is

formed using a circular knitting machine. *Id.* at 1348–49.

The central tenet of our written description jurisprudence—that the disclosure must be read from the perspective of a person of skill in the art—further recognizes that the disclosure need not describe a limitation *in haec verba*. *See*, *e.g.*, *All Dental Prodx, LLC v. Advantage Dental Prod., Inc.*, 309 F.3d 774, 779 (Fed. Cir. 2002) (citing *Eiselstein v. Frank*, 52 F.3d 1035, 1039 (Fed. Cir. 1995) ("[T]he failure of the specification to specifically mention a limitation that later appears in the claims is not a fatal one when one skilled in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented."); *see also Ariad*, 598 F.3d at 1351.

The Manual of Patent Examining Procedure ("MPEP") similarly provides for written description in various forms. In addition to stating that the "mere absence of a positive recitation" is not enough, the MPEP also correctly states that no specific form of disclosure is required and provides for implicit written description.[1] MPEP § 2173.05(i) states that "a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of descriptive support." And MPEP § 2163 states that "newly added claims or claim limitations must be supported in the specification through express, *implicit*, or inherent disclosure." MPEP § 2163 (emphasis added).

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[1] I cite the MPEP, not because the court is bound by it but because I find its reasoning informative and persuasive.

What is critical is how a person of skill in the art would read the disclosure—not the exact words used.

In other words, context and the knowledge of those skilled in the art matter. And, as the Supreme Court has made clear, when assessing what the written description reveals to a skilled artisan, common sense also matters. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007) (holding that, in an obviousness analysis, "[r]igid preventative rules that deny factfinders recourse to common sense, however, are neither necessary under our case law nor consistent with it").

II

Here, the district court conducted "an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art" and found sufficient written description in the EAE model and the Prophetic Trial. J.A. 37 (citing *Ariad*, 598 F.3d at 1351). The district court found that the "Prophetic Trial describes giving a 'daily dosage of 0.5 . . . mg' fingolimod to treat RRMS, started 'initially.' " J.A. 26 ¶ 62 (quoting '405 patent col. 11 ll. 8–13). The court found, crediting expert testimony, that, "[i]f a loading dose were directed, the Patent would say that a loading dose should be administered 'initially.' " J.A. 26 ¶ 62 (citing J.A. 23334–35 (Tr. 756:16–757:8); J.A. 23441–42 (Tr. 863:22–864:18)). The district court thus made the unremarkable, and factually supported, determination that "starting with a daily dose plainly implies that there is no loading dose." J.A. 27. Similarly, the district

court found that the "EAE example discloses a dosing regimen which does not involve a loading dose." J.A. 27 ¶ 64 (citing J.A. 23345 (Tr. 767:3–5); J.A. 22793 (Tr. 215:16–21)). The district court held that the description in the specification of administration of a daily dose "would tell a person of skill that loading doses are excluded from the invention." J.A. 26 ¶ 61. The court also found that "[a] loading dose is necessarily a higher-than daily dose." J.A. 27 ¶ 63 (Tr. 766:4–766:6). Finally, the court found that, while the patent describes alternate dosing regimens, such as "intermittent dosing," it does not describe administering those regimens with loading doses. J.A. 27 ¶ 65. Thus, the district court concluded, "[t]he EAE model and the Prophetic Trial . . . indicate to a person of ordinary skill that the claimed invention did not include the administration of a loading dose." J.A. 37–38. The cited passages of the specification provide clear disclosure of a dosing regimen that is not dependent upon or subject to the administration of a loading dose.

The majority finds that the word "initially" "speaks to the initial length of treatment not the dosage with which treatment begins." Maj. at 7–8. Here, the district court found that the "Prophetic Trial describes giving a 'daily dosage of 0.5 . . . mg' fingolimod to treat RRMS, started 'initially.' " J.A. 26. While other interpretations of the word "initially" might be reasonable, the language, used in context, also supports the district court's finding that the written description discloses excluding a loading dose. We are not free to substitute our own factual findings for those of the district

court absent clear error because "a district court judge who has presided over, and listened to, the entire proceeding has a comparatively greater opportunity to gain the necessary 'familiarity with specific scientific problems and principles,' . . . than an appeals court judge who must read a written transcript or perhaps just those portions referenced by the parties." *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 319 (2015) (quoting *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 610 (1950)).

The majority asserts that the disclosure of a daily dosage cannot amount to a disclosure that there can be no loading dose, because such a finding is at odds with the prosecution history and the fact that the examiner allowed the claims only after the no-load limitation was added. Maj. at 10. According to the majority, if reciting a "daily dosage" necessarily excluded a loading dose, there would have been no reason to add the no-dose limitation. *Id.* at 10:19-22. But Novartis, in adding the no-load limitation was doing no more than what applicants regularly do to secure allowance in making explicit that which was implicit prior to the amendment. There is no basis to read more into the prosecution history and certainly no basis to negate the clear disclosure of a "daily dosage" and the expert testimony describing the understanding of that expression to skilled artisans.

The majority asserts that "the question is not whether the patentee intended there to be a loading dose; the question is whether the patentee precluded the use of a loading dose." Maj. at 11. I submit that the

question posed by the majority is misstated. The question is not whether the patentee precluded the use of a loading dose but whether the claim language that precludes the administration of a loading dose is supported by the written description passages that disclose the effective administration of nothing more than a "daily dose." In context, that disclosure, according to the testimony of the Novartis's experts, implies the absence of a loading dose to the ordinarily skilled artisan. That is all that is required.

Finally, the majority finds significant tension between the district court's finding that the specification's disclosure excludes a loading dose, but the Kappos 2006 abstract does not. Maj. at 9. I see no tension or legal inconsistency in the district court's treatment of the Kappos 2006 abstract. As the court explained, Kappos was an abstract with no presumption of enablement or completeness, and it in any event did not include the animal trials that form an important part of Novartis's arguments with respect to the '405 patent. As importantly, the district court also found no evidence that Kappos 2006 was publicly available before the priority date because there was no evidence of public access. J.A. 28.

For all these reasons, I respectfully dissent.

APPENDIX B

United States Court of Appeals
for the Federal Circuit

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff-Appellee

v.

ACCORD HEALTHCARE, INC., AUROBINDO PHARMA LTD., AUROBINDO PHARMA USA, INC., DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., EMCURE PHARMACEUTICALS LTD., HERITAGE PHARMACEUTICALS INC., GLENMARK PHARMACEUTICALS INC., USA, GLENMARK PHARMACEUTICALS LIMITED, HETERO USA, INC., HETERO LABS LIMITED UNIT-V, HETERO LABS LIMITED, MYLAN PHARMACEUTICALS, INC., PRINSTON PHARMACEUTICAL INC., STRIDES GLOBAL PHARMA PRIVATE LIMITED, STRIDES PHARMA, INC., TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD., ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., APOTEX INC., APOTEX CORP., SUN PHARMACEUTICAL INDUSTRIES, LTD., SUN PHARMACEUTICAL INDUSTRIES INC., SUN PHARMA GLOBAL FZE,
Defendants

HEC PHARM CO., LTD., HEC PHARM USA INC.,
Defendants-Appellants

2021-1070

Appeal from the United States District Court for the District of Delaware in No. 1:18-cv-01043-KAJ, Circuit Judge Kent A. Jordan.

Decided: January 3, 2021

JANE M. LOVE, Gibson, Dunn & Crutcher LLP, New York, NY, argued for plaintiff-appellee. Also represented by PAUL E. TORCHIA, ROBERT TRENCHARD.

PAUL SKIERMONT, Skiermont Derby LLP, Dallas, TX, argued for defendants-appellants. Also represented by SARAH ELIZABETH SPIRES; MIEKE K. MALMBERG, Los Angeles, CA.

Before MOORE, *Chief Judge*, LINN and O'MALLEY, *Circuit Judges*.

Opinion for the court filed by *Circuit Judge* O'MALLEY.

Dissenting opinion filed by *Chief Judge* MOORE

O'MALLEY, *Circuit Judge*.

HEC Pharm Co., Ltd. and HEC Pharm USA Inc. (collectively, "HEC") appeal from a district court bench

trial in which the court found that a patent assigned to Novartis Pharmaceuticals Corp. ("Novartis"), U.S. Patent No. 9,187,405 ("the '405 patent"), is not invalid and that HEC's Abbreviated New Drug Application ("ANDA") infringes. HEC argues that the district court erred in finding that the '405 claims do not fail the written description requirement of 35 U.S.C. § 112(a). Because we do not discern any clear error in the district court's decision, we affirm.

I. BACKGROUND

Novartis markets a 0.5 mg daily dose of fingolimod hydrochloride under the brand name Gilenya. The medication is used to treat relapsing remitting multiple sclerosis ("RRMS"), a form of multiple sclerosis ("MS"). MS is a debilitating immune-mediated demyelinating disease in which the immune system attacks the myelin coating the nerves in the central nervous system. Most MS patients initially present as RRMS patients, but many eventually develop a secondary progressive form of MS, causing them to experience growing disability. There is currently no cure for MS. The disease is managed by reducing or preventing relapses and thereby slowing disability.

HEC filed an ANDA seeking approval to market a generic version of Gilenya. Novartis sued, alleging that HEC's ANDA infringes all claims of the '405 patent.[1]

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[1] Novartis sued several other defendants who had also filed ANDA applications. The cases as to those other defendants all

A. The '405 Patent

The '405 patent claims methods to treat RRMS with fingolimod (also known as FTY720 and 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol in the '405 patent) or a fingolimod salt, such as fingolimod hydrochloride (also known as Compound A in the '405 patent), at a daily dosage of 0.5 mg without an immediately preceding loading dose. '405 patent col. 12 ll. 49–55.

A loading dose is a higher than daily dose "usually given 'as the first dose.'" J.A. 27 (¶ 63) (quoting J.A. 23125 (Tr. 547:12–18) and citing J.A. 23344 (Tr. 766:4–6)). Both parties' experts agreed with this definition. J.A. 23125 (547:12–18) (HEC's expert, Dr. Hoffman, testifying that "a loading dose is a higher-than-therapeutic level dose, usually given . . . as the first dose in order to get therapeutic levels up quickly . . . and it's usually for more acute situations"); J.A. 23344 (Tr. 766:4–6) (Novartis's expert, Dr. Steinman, agreeing that "a loading dose is a higher-than-daily dose"). It is undisputed that loading doses were well-known in the medical field generally and in the prior art. And the experts in this case agree that loading doses are used for some medicaments used in connection with MS.

The '405 patent has six claims. Claim 1 of the '405 patent recites:

> A method for reducing or preventing or alleviating relapses in Relapsing-Remitting multiple sclerosis in a subject in need thereof,

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settled or were stayed prior to trial, which proceeded only as to HEC.

> comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

Claims 3 and 5 are similar but are directed to a "method of treating" RRMS and a "method of slowing progression of" RRMS, respectively, rather than a "method for reducing or preventing or alleviating relapses in" RRMS. *Id.* col. 12 ll. 59–64, col. 13 ll. 1–6. Claims 2, 4, and 6 are dependent claims that limit the methods of claims 1, 3, and 5, respectively, to administration of 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride, i.e., fingolimod hydrochloride. *Id.* col. 12 ll. 56–58, col. 12 ll. 65–67, col. 13 ll. 7–9.

The '405 patent was filed on April 21, 2014. It claims priority to a British patent application that was filed on June 27, 2006. The parties, for the most part, focus their discussion on the specification of the '405 patent, despite HEC's argument that the inventors did not possess the invention *as of the 2006 priority date.* HEC's argument that the 2006 application does not contain adequate written description of the '405 claims requires reference to the 2006 application itself. Thus, we find it necessary to look to the specification of the 2006 priority application, despite the parties' failure to fully explain the contents of that application. Although the specifications are different from each other, they are, in all aspects relevant to this appeal, substantively similar.

The specifications of the '405 patent and the 2006 priority application both describe the use of a class of S1P receptor modulators, including fingolimod, to treat or prevent "neo-angiogenesis associated with a demyelinating disease, e.g. multiple sclerosis." '405 patent col. 1 ll. 5–8; J.A. 23751. The specifications each identify fingolimod hydrochloride (Compound A) as a particularly preferred compound within the class of S1P receptor modulators. '405 patent col. 8 ll. 17–30; J.A. 23759–60.

Both specifications describe the results of an Experimental Autoimmune Encephalomyelitis ("EAE") experiment. '405 patent col. 10 ll. 32-col. 11 ll. 2; J.A. 23762–63. In the EAE experiment, a disease that mimics RRMS was induced in Lewis rats.[2] The rats suffered acute disease within 11 days after immunization, with almost complete remission around day 16 and relapse around day 26. The specifications report that an S1P receptor modulator, e.g., Compound A (fingolimod hydrochloride) "significantly blocks disease-associated neo-angiogenesis when administered to the animals at a dose of from 0.1 to 20 mg/kg p.o."[3] '405 patent col. 10 ll. 61–64; J.A. 23763. They further report that disease relapse was completely inhibited in rats to which Compound A was "administered daily at a dose of 0.3 mg/kg" or "administered p.o. at 0.3

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[2] Lewis rats are inbred laboratory rats used to study disease. *Inbred Rats*, Charles River, https://www.criver.com/sites/default/files/resources/InbredRatsDatasheet.pdf (last visited November 5, 2021).

[3] P.o. indicates oral administration.

mg/kg every 2nd or 3rd day or once a week." '405 patent col. 10 ll. 64-col. 11 ll. 3; J.A. 23763.

Both specifications then describe a prophetic human clinical trial ("Prophetic Trial").[4] '405 patent col. 11 ll. 3–38; J.A. 23763–64. The Prophetic Trial describes a trial in which RRMS patients would receive 0.5, 1.25, or 2.5 mg of an S1P receptor modulator, e.g., Compound A (fingolimod hydrochloride), per day for two to six months. '405 patent col. 11 ll. 8–14; J.A. 23763. The specifications do not mention a loading dose associated with the Prophetic Trial. '405 patent col. 11 ll. 8–14; J.A. 23763.

Both specifications then describe a wide range of potential dosages, which "will vary depending upon, for example, the compound used, the host, the mode of administration and the severity of the condition to be treated." '405 patent col. 11 ll. 20–24; J.A. 23764. Those potential dosages include a "preferred daily dosage range [of] about from 0.1 to 100 mg" and "a dose of 0.5 to 30 mg [of Compound A] every other day or once a week." '405 patent col. 11 ll. 24–38; J.A. 23764.

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[4] Prophetic trials explain how a drug would be administered and how a patient given that drug should be monitored in a clinical trial. Prophetic trials are not clinical trials that are performed; they are merely described on paper. Prophetic trials are sometimes used in patent applications because clinical trials are expensive and time consuming.

B. The District Court Proceedings

After a four-day bench trial, the district court found that HEC's ANDA product would infringe claims 1–6 of the '405 patent. The court also found that HEC had not shown that the '405 patent is invalid for (1) insufficient written description for the no-loading-dose limitation and for the claimed 0.5 mg daily dose or (2) anticipation. HEC appeals the district court's findings as to written description for the 0.5 mg daily dose and no-loading-dose limitations.

With respect to the written description for the claimed 0.5 mg daily dose, the district court found that a skilled artisan would understand that the inventors possessed a 0.5 mg daily dose based on one of the successful doses in the EAE experiment results, 0.3 mg/kg weekly. The court credited the testimony of two of Novartis's expert witnesses, Dr. Lawrence Steinman, M.D., and Dr. William Jusko, Ph.D., to make the leap from a 0.3 mg/kg weekly rat dosage to a 0.5 mg daily human dosage. The court noted that the 0.5 mg daily dose is also illustrated in the Prophetic Trial. The district court concluded that there was sufficient written description for the 0.5 mg daily dosage limitation.

With respect to the written description for the "absent an immediately preceding loading dose" limitation, the district court again found sufficient written description in the EAE model and the Prophetic Trial. Neither the Prophetic Trial nor the EAE model recite a loading dose. The district court found that the "Prophetic Trial describes giving a 'daily dosage of 0.5 . . .

mg' fingolimod to treat RRMS, started 'initially.'" J.A. 26 (quoting '405 patent col. 11 ll. 8–13). The court found, crediting expert testimony, that, "[i]f a loading dose were directed, the Patent would say that a loading dose should be administered 'initially.'" J.A. 26 (citing J.A. 23334–35 (Tr. 756:16–757:8); J.A. 23441–42 (Tr. 863:22–864:18)). Similarly, the district court found that the "EAE example discloses a dosing regimen which does not involve a loading dose." J.A. 27 (citing J.A. 23345 (Tr. 767:3–5); J.A. 22793 (Tr. 215:16–21)). Finally, the court found that, while the patent describes alternate dosing regimens, such as "intermittent dosing," it does not describe administering those regimens with loading doses. J.A. 27. Thus, the district court concluded, "[t]he EAE model and the Prophetic Trial . . . indicate to a person of ordinary skill that the claimed invention did not include the administration of a loading dose," and, thus, the patent provides sufficient written description of the negative limitation. J.A. 37–38.

HEC appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

II. Discussion

On appeal, HEC challenges the district court's decisions concerning the '405 patent's written description of the 0.5 mg daily dose limitation and the no-loading-dose negative limitation. "Whether a claim satisfies the written description requirement is a question of fact that, on appeal from a bench trial, we review for clear error." *Allergan, Inc. v. Sandoz Inc.*,

796 F.3d 1293, 1308 (Fed. Cir. 2015) (quoting *Alcon Rsch. Ltd. v. Barr Lab'ys, Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014)). Under the clear error standard, we will not overturn the district court's factual finding unless we have a " 'definite and firm conviction' that a mistake has been made." *Nuvo Pharms. (Ireland) Designated Activity Co. v. Dr. Reddy's Lab'ys Inc.*, 923 F.3d 1368, 1376 (Fed. Cir. 2019) (quoting *Scanner Techs. Corp. v. ICOS Vision Sys. Corp. N.V.*, 528 F.3d 1365, 1374 (Fed. Cir. 2008)).

The written description requirement is found in section 112 of the patent statute, which provides that the patent's specification must contain "a written description of the invention, and of the manner and process of making and using it."[5] 35 U.S.C. § 112(a). A specification that "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date" has adequate written description of the claimed invention. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.*

HEC challenges the district court's decisions concerning the '405 patent's written description of two limitations: the 0.5 mg daily dose limitation and the no-loading-dose negative limitation.

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[5] 35 U.S.C. § 112(a) also contains the separate "enablement" requirement, which is not at issue in this appeal.

Despite arguing that the inventors did not possess the claimed subject matter in 2006, HEC bases its arguments, not on the 2006 priority application's written description, but on the '405 patent's specification—leaving it to this court to independently search the 2006 priority application for written description of the claims. HEC's confusion is ultimately of no moment, as we find that the claims have adequate written description support in portions of the '405 specification which also appear in the 2006 priority application.[6]

A. Written Description for the Dosage Limitation

HEC argues that, as of the 2006 priority date, the inventors did not possess a 0.5 mg daily dose of fingolimod. It argues that, as of that date, 0.5 mg/day was considered too low to be effective to treat RRMS. It describes Novartis's calculation of the 0.5 mg/day human dose as derived from the lowest disclosed dose in the rat EAE model described in the specification as "undisclosed mathematical sleights of hand." Appellant's Br. 7. And it argues that the Prophetic

[6] Both parties wrongly assume that, if the 2006 priority application lacks sufficient written description of the '405 patent's claims, those claims are invalid. If the 2006 priority application lacks sufficient written description for the '405 patent's claims, the '405 patent's claims are not automatically rendered invalid; they are merely deprived of the 2006 priority date. *See* 35 U.S.C. § 119; *see also Paice LLC v. Ford Motor Co.*, 881 F.3d 894, 906 (Fed. Cir. 2018) ("For claims to be entitled to a priority date of an earlier-filed application, the application must provide adequate written description support for the later-claimed limitations.").

Trial, which lists a 0.5 mg daily dose along with two other dosages, does not provide sufficient written description of the 0.5 mg dose. Finally, it asserts that "blaze marks" directing a skilled artisan to the 0.5 mg daily dose are absent from the '405 patent.

We do not find HEC's arguments convincing. The Prophetic Trial and the EAE model provide sufficient written description to show that, as of the priority date, the inventors possessed a 0.5 daily fingolimod dosage as claimed in the '405 patent. The Prophetic Trial describes dosing RRMS patients with fingolimod hydrochloride at daily dosages of 0.5, 1.25, or 2.5 mg. '405 patent col. 11 ll. 8–16. The Prophetic Trial's disclosure of two other dosages does not detract from the written description of the claimed dose. Nor do disclosures of dosage ranges in other areas of the specification lead away from the claimed dose.

The rat EAE model describes additional information which provides further written description for the 0.5 mg/day limitation. The EAE model describes a dosage of 0.3 mg/kg per week as effective to "fully block[] disease-associated angiogenesis and completely inhibit[] the relapse phases." '405 patent col. 10 ll. 64-col. 11 ll. 2. The district court credited the testimonies of Dr. Steinman and Dr. Jusko to arrive at the claimed 0.5 mg/day human dosage from the EAE experiment's 0.3 mg/kg per week rat dosage. Those experts both testified that a skilled artisan would have converted the lowest daily rat dose described in the EAE experiment (0.3 mg/kg weekly) to a daily dose (0.042 mg/kg daily). J.A. 24 (citing J.A. 23325–26

(Tr. 747:6–748:19); J.A. 23443 (Tr. 865:12–24); J.A. 23482 (Tr. 904:2–18)). The district court found, again based on expert testimony, that a skilled artisan "would immediately recognize that 0.3 mg/kg weekly (0.042 mg/kg daily) in rats" is approximately 60% lower "than the lowest known effective dose in the prior art (0.1 mg/kg daily)." J.A. 24–25 (citing J.A. 23440–41 (Tr. 862:25–863:21)). It found that a skilled artisan "would understand that the EAE results in the '405 Patent therefore demonstrate that a proportionally lower dose (again, roughly 60% lower) could be effective in humans." J.A. 25 (citing J.A. 23443–45 (Tr. 865:4–867:4); J.A. 23480–85 (Tr. 902:17–907:8)). It further found that a skilled artisan "would understand that the inventors translated the lowest dose that had ever been seen as effective from their EAE experiment (0.3 mg/kg once per week) to the 0.5 dose." J.A. 25 (citing J.A. 23356–57 (Tr. 778:25–779:14)).

HEC attacks the expert testimony underlying the district court's determination that the EAE experiment describes a 0.5 mg daily human dose as "undisclosed mathematical sleights of hand." Appellant's Br. 7. We disagree. A "disclosure need not recite the claimed invention *in haec verba*." *Ariad*, 598 F.3d at 1352. The disclosure need only "clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed." *Id.* at 1351. To accept HEC's argument would require us to ignore the perspective of the person of ordinary skill in the art and require literal description of every limitation, in violation of our precedent. We find no clear

error in the district court's reliance on expert testimony in finding description of the 0.5 mg daily human dose in the EAE experiment results.

We also reject HEC's argument that the '405 patent does not have necessary "blaze marks" pointing to the 0.5 mg daily dose. "Blaze marks" directing an investigator of ordinary skill in the art to the claimed species from among a forest of disclosed options are not necessary in this case. In cases where the specification describes a broad genus and the claims are directed to a single species or a narrow subgenus, we have held that the specification must contain " 'blaze marks' that would lead an ordinarily skilled investigator toward such a species among a slew of competing possibilities." *Novozymes v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1349 (Fed. Cir. 2013).

"Blaze marks" are not necessary where the claimed species is expressly described in the specification, as the 0.5 mg daily dosage is here. *See*, *e.g.*, *Snitzer v. Etzel*, 59 CCPA 1242, 465 F.2d 899, 902 (1972) (finding that interference counts directed to the activation of a glass laser with trivalent ytterbium ions were adequately described by a specification listing fourteen materials which may be used as active laser ingredients, including trivalent ytterbium, and noting that "there would seem to be little doubt that the literal description of a species provides the requisite legal foundation for claiming that species"). The '405 patent does not contain the laundry-list-type disclosures that we have found require guidance to direct a skilled artisan to the claimed species—it contains the Prophetic

Trial listing three doses, 0.5, 1.25, and 2.5 mg/day. While other sections of the specification disclose larger ranges of potential doses for S1P receptor modulators, e.g., 0.1 to 100 mg/day doses, those disclosures do not diminish the literal description of the 0.5 mg/day dose in the Prophetic Trial. All described dose ranges include the 0.5 mg/day dose. And smaller dosage ranges, such as 0.5–30 mg/day, are disclosed for fingolimod hydrochloride. Even if blaze marks were required in this case, the Prophetic Trial and 0.5–30 mg/day dosage range would provide a skilled artisan more than sufficient guidance to direct them to the claimed 0.5 mg/day dose.

Much of HEC's argument is directed to its assertion that no one, including the inventors, knew that a 0.5 mg/day dose would be effective as of the 2006 priority date. That argument fails for two reasons. First, efficacy is not a requirement of the claims. The claims require only administration of a 0.5 mg/day dose for, *inter alia*, treatment purposes. The district court found that the purpose limitations are adequately described, and HEC has not appealed that finding. Thus, cases such as *Nuvo Pharms.*, 923 F.3d 1368, in which this court found that claims directed to an amount of uncoated PPI that is *effective* to raise the gastric pH to at least 3.5 were not adequately described by a specification that "provides nothing more than the mere claim that uncoated PPI might work" where skilled artisans "would not have thought it would work," are distinguishable. *See id.* at 1381. Second, as explained above, the EAE model provides evidence that the

inventors knew that a 60% lower dose would be effective.

For these reasons, we find no clear error in the district court's holding that the 0.5 mg/day dosage limitation is adequately described. The district court's holding is supported by the specification and ample expert testimony interpreting that specification.

B. Written Description for the Negative Limitation

HEC argues that there is no written description of the negative limitation because the '405 specification contains no recitation of a loading dose "or its potential benefits or disadvantages at all." Appellant's Br. 40. It further argues that the district court's finding of written description of the negative limitation within the '405 specification contradicts the district court's finding that Kappos 2006, which is similarly silent as to loading doses, does not anticipate the claims. We find both arguments unavailing.

It is well established that there is no "new and heightened standard for negative claim limitations." *Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1356 (Fed. Cir. 2015). We are aware of no case that suggests otherwise. And, while HEC asserts that "[i]t is well-settled law that silence alone cannot serve as a basis for" a negative limitation, Appellant's Br. 41, HEC identifies no case that actually supports that proposition. To the contrary, we repeatedly have resisted imposition of heightened written description standards for negative limitations, such as that urged by HEC.

For example, in *Santarus, Inc. v. Par Pharmaceutical, Inc.*, we found that claims directed to a method of treatment with a pharmaceutical composition containing no sucralfate were adequately described by a specification that explained that, although sucralfate is "possibly the ideal agent for stress ulcer prophylaxis," it was known to have occasional adverse effects. 694 F.3d 1344, 1350–51 (Fed. Cir. 2012). In *Santarus*, as in this case, there was expert testimony providing a person of ordinary skill's understanding of the patent specification. *See id.* at 1351. The expert testimony in *Santarus* showed that "a person of ordinary skill in this field . . . would have understood from the specification that disadvantages of sucralfate may be avoided by the [claimed] formulation." *Id.* We explained that "[n]egative claim limitations are adequately supported when the specification describes a reason to exclude the relevant limitation." *Id.* We did not hold that a specification *must* describe a reason to exclude a negative limitation. A specification that describes a reason to exclude the relevant negative limitation is but one way in which the written description requirement may be met.

In *In re Bimeda Research. & Development Ltd.*, we held that a claim that excluded a specific anti-infective, acriflavine, was not adequately described by a disclosure that was inconsistent with the exclusion of acriflavine but not other anti-infectives or antibiotics. 724 F.3d 1320, 1324 (Fed. Cir. 2013). The claim at issue in *Bimeda* was directed to a method of preventing mastitis in dairy cows by sealing the teat canal of a cow's

mammary gland with a seal formulation that excludes acriflavine. Other claims in the same patent excluded all anti-infective agents. We noted that the patent repeatedly distinguished the invention as able to prevent mastitis without the use of antibiotics. Based on the written description's consistent description of the invention's non-antibiotic approach to preventing mastitis, we concluded that the patent's disclosure was "inconsistent with a claim which excludes acriflavine, but *not* the presence of other antiinfectives or antibiotics." *Id.* (citation and quotation marks omitted). We did not require that the specification describe a reason to exclude acriflavine specifically, but, rather, found only that a negative limitation which is inconsistent with the disclosure is not adequately described.

In *Inphi*, we confirmed that the written description requirement is satisfied where "'the essence of the original disclosure' conveys the necessary information—'regardless of *how* it' conveys such information, and regardless of whether the disclosure's 'words [a]re open to different interpretation[s].'" 805 F.3d at 1354 (quoting *In re Wright*, 866 F.2d 422, 424–25 (Fed. Cir. 1989) (citation and internal quotation marks omitted)). We explained that "*Santarus* simply reflects the fact that the specification need only satisfy the requirements of § 112, paragraph 1 as described in this court's existing jurisprudence[.]" *Id.* at 1356. And we noted that the "'reason' required by *Santarus* is provided, for instance, by properly describing alternative features of the patented invention." *Id.* (citing *In re Johnson*, 558 F.2d 1008, 1019 (C.C.P.A. 1977)).

In *Inphi*, we found that substantial evidence supported the Patent Trial and Appeal Board's ("Board") finding that a negative limitation which had been added during prosecution ("DDR chip selects that are not CAS, RAS, or bank address signals") was adequately described by an original specification which did not expressly articulate a reason to exclude RAS and CAS signals. We found the Board's decision was supported by evidence of (1) standards set by the Joint Electron Device Engineering Council, a global standard setting body for the microelectronics industry, incorporated by reference in the patent, which specify that DDR signals, including CS, RAS, CAS, and bank address signals, are distinct from each other; (2) a table in the specification which excludes RAS and CAS signals; and (3) various passages from the specification, including a figure which distinguishes chip select signals, command signals (including RAS and CAS signals) and bank address signals. We concluded that the specification's disclosure of alternative features was sufficient to satisfy the written description standard for the negative limitation. *Id.* at 1357.

In *Nike, Inc. v. Adidas AG*, we reiterated that *Santarus* did not create a heightened standard for written description of negative limitations. 812 F.3d 1326, 1348 (Fed. Cir. 2016), *overruled on other grounds by Aqua Prods., Inc. v. Matal*, 872 F.3d 1290 (Fed. Cir. 2017). We stated that negative limitations, like all other limitations, are held to "the customary standard for the written description requirement." *Id.* In *Nike*, we found a limitation of "flat knit edges," which

Adidas characterized as a negative limitation, was adequately described by three figures in the specification depicting the claimed textile element which Nike's expert opined could be made using flat knitting in contrast to another figure's textile element which is formed using a circular knitting machine. *Id.* at 1348–49.

Similarly, in *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, Judge Bryson, sitting by designation in the Eastern District of Texas, explained that the law does not require that the disclosure explain a negative limitation. 276 F. Supp. 3d 629, 657–58 (E.D. Tex. 2017), *aff'd*, 739 F. App'x 643 (Fed. Cir. 2018). Judge Bryson explained, citing *Bimeda*, that "[w]hat is prohibited is a negative limitation that is contrary to the thrust of the invention." *Id.* at 658. He noted that "a patentee can choose to claim any particular embodiments identified in the specification and exclude others, without explanation, as long as the claim does not indicate to persons of skill that it covers embodiments inconsistent with, and therefore unsupported by, the disclosure." *Id.*

In asserting that "silence alone cannot serve as a basis for" a negative limitation, Appellant's Br. 41, HEC attempts to create a new heightened written description standard for negative limitations. In doing so, it ignores a central tenet of our written description jurisprudence—that the disclosure must be read from the perspective of a person of skill in the art—as well as precedent stating that the disclosure need not describe a limitation *in haec verba*. *See*, *e.g.*, *All Dental*

Prodx, LLC v. Advantage Dental Prod., Inc., 309 F.3d 774, 779 (Fed. Cir. 2002) ("[T]he failure of the specification to specifically mention a limitation that later appears in the claims is not a fatal one when one skilled in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented.") (citing *Eiselstein v. Frank*, 52 F.3d 1035, 1039 (Fed. Cir. 1995)); *see also Ariad*, 598 F.3d at 1351. In other words, context and the knowledge of those skilled in the art matter. And, as the Supreme Court has made clear, when assessing what the written description reveals to a skilled artisan, common sense also matters. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007) (holding that, in an obviousness analysis, "[r]igid preventative rules that deny factfinders recourse to common sense, however, are neither necessary under our case law nor consistent with it").

The dissent notes that the Manual of Patent Examining Procedure ("MPEP")[7] states: "The mere absence of a positive recitation is not a basis for an exclusion." MPEP § 2173.05(i). As the dissent puts it—"silence alone is insufficient." Dissent at 4. Both the MPEP and the dissent are correct in their statement of the law: the "*mere absence* of a positive recitation" is not enough and "silence *alone* is insufficient." But the dissent, like HEC, ignores that it is how a skilled artisan reads a disclosure that matters. Written description may take

[7] The MPEP is not binding on this court but may be persuasive.

any form, so long as a skilled artisan would read the disclosure as describing the claimed invention.

Our case law makes clear that "[c]ompliance with the written description requirement is essentially a fact-based inquiry that will 'necessarily vary depending on the nature of the invention claimed.'" *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 963 (Fed. Cir. 2002) (quoting *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1562 (Fed. Cir. 1991)). The MPEP similarly provides for written description in various forms. In addition to stating that the "mere absence of a positive recitation" is not enough, the MPEP also correctly states that no specific form of disclosure is required and provides for implicit written description. MPEP § 2173.05(i) states that "a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of descriptive support." And MPEP § 2163 states that "newly added claims or claim limitations must be supported in the specification through express, *implicit*, or inherent disclosure." MPEP § 2163 (emphasis added). What is critical is how a person of skill in the art would read the disclosure—not the exact words used.

HEC and the dissent urge us to elevate form over substance by creating a new rule that a limitation which is not expressly recited in the disclosure is never adequately described, regardless of how a skilled artisan would read that disclosure. As we have several times before, we reject the invitation to create a heightened written description standard for negative limitations. As with all other limitations, the negative

limitation here must be accompanied by an original disclosure which *conveys to a person of ordinary skill* that the inventor was in possession of the claimed invention. *See Ariad*, 598 F.3d at 1351. And, as in all other written description challenges, HEC was required to show by clear and convincing evidence that the negative limitation was not adequately described. The district court did not clearly err in finding that HEC failed to do so.

In determining that there is adequate written description of the negative limitation, the district court correctly, and quite carefully, conducted "an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art" as required by our precedent. *See Ariad*, 598 F.3d at 1351. We review the evidence cited by the district court below and discern no clear error in the court's analysis or conclusions.

The Prophetic Trial describes giving RRMS patients fingolimod hydrochloride "at a daily dosage of 0.5, 1.25 or 2.5 mg p.o." '405 patent col. 11 ll. 8–9. It further states that: "Initially patients receive treatment for 2 to 6 months." *Id.* col. 11 ll. 13–14. Dr. Steinman, one of Novartis's expert witnesses, testified from the perspective of a skilled artisan that, if the Prophetic Trial included a loading dose, the patent would explicitly state as much:

> "[T]here were two places where if there were going to be a loading dose, you would explicitly state it.

> . . . .
>
> So the first place one might explicitly say there was—there was a preceding loading dose is when you described the daily dosage, the reason being a loading dose would occur before the first daily dose.
>
> The second place is even more dramatic, because they say, "Initially patients received treatment for 2 to 6 months." So now they're really zooming in on Day 1, what is that treatment, it's a daily dose of 0.5.
>
> So there were two perfectly logical places that if there was going to be a loading dose, it would have been stated.
>
> . . . .
>
> That's where you would put it if you were going to give a loading dose.

J.A. 23343 (Tr. 765:2–25).

Similarly, Dr. Fred Lublin, Ph.D., another expert testifying for Novartis, testified that a person of skill in the art "would have viewed the patent as a document, as a complete document, that should give you all the information you need to carry out the claims, and that information of having a loading dose is not there, and what's instead there is examples of daily dose, daily dose, daily dose." J.A. 22791 (Tr. 213:6–15). Dr. Lublin testified that a "loading dose is a greater than normal dose that you give until you return to a maintenance dose" and a loading dose is "not a daily dose." J.A. 22792 (Tr. 214:1–9). He further testified that

"[o]ne would expect in a patent that if there was going to be a loading dose, it would be specified." J.A. 22793 (Tr. 215:5–8). And a third expert testifying for Novartis, Dr. Jusko, similarly testified that, from the perspective of a person of skill in pharmacology, the Prophetic Trial has a "specified initial regimen that does not include a loading dose." J.A. 23442 (Tr. 864:14–16).

The district court credited this expert testimony, as well as the testimony from HEC's own expert, Dr. Paul Hoffman, M.D., who agreed that "a loading dose is a higher-than-therapeutic level dose, usually given . . . as the first dose." J.A. 23125 (Tr. 547:14–18); J.A. 27. Based on that evidence, the court concluded that the "absence of an immediately preceding loading dose from the specification, and from the Prophetic Trial, would tell a person of skill that loading doses are excluded from the invention." J.A. 26. We discern no clear error in that finding. The district court further noted that the rat EAE experiment does not describe a loading dose. J.A. 26. It again credited the testimony of multiple expert witnesses who testified that the EAE model did not include a loading dose. J.A. 26. Dr. Jusko, in response to a question about whether there are any loading doses in the EAE model, stated: "Not that I'm aware of." J.A. 22793 (Tr. 215:16–21). Dr. Steinman similarly testified that no loading dose was used in the EAE experiment. J.A. 23345 (Tr. 767:3–5). HEC's own expert witness, Dr. Hoffman, testified that the EAE model does not talk about a loading dose. J.A. 23209 (Tr. 631:18–22). Based on both the specification's disclosure of the rat EAE model and the ample expert

testimony providing evidence of how a person of ordinary skill would read that disclosure, the district court concluded that the "EAE example discloses a dosing regimen which does not involve a loading dose." J.A. 27. Finally, the district court noted that, while the patent "describes alternative dosing regimens, like 'intermittent dosing,' [it] does not describe loading doses." J.A. 27.

The district court concluded that the "EAE model and the Prophetic Trial . . . both indicate to a person of ordinary skill that the claimed invention did not include the administration of a loading dose." J.A. 37–38. We are not left with the "definite and firm conviction" that the district court made a mistake in coming to this conclusion. *See Nuvo Pharms.*, 923 F.3d at 1376 (quoting *Scanner Techs.*, 528 F.3d at 1374). To the contrary, the district court's conclusion appears wholly correct. To arrive at the opposite conclusion would require us to disregard the perspective of a person of skill in the art—something our precedent simply does not allow. *See Ariad*, 598 F.3d at 1351.

We also find unpersuasive HEC's argument that the district court's written description decision contradicts its determination that the '405 patent is not anticipated by Kappos 2006. HEC notes that neither Kappos 2006 nor the '405 patent's specification explicitly state that a loading dose should not be administered. But HEC's argument ignores the differences between the two district court findings and ignores the differences between the disclosures of Kappos 2006 and the '405 specification.

As a granted patent, the '405 patent is presumed valid. Thus, it is also presumed to have a complete written description. *See Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195 (Fed. Cir. 1999) ("The presumption of validity includes a presumption that the patent complies with § 112."). No such presumption applies to disclosures of a prior art reference that is not itself a granted patent, such as Kappos 2006. Further, the perspective of a person of skill in the art is important in both the written description and the anticipation inquiries. And, in this case, the district court credited the testimony of two expert witnesses, Dr. Lublin and Dr. Steinman, who testified that a person of skill in the art would not presume that the Kappos 2006 abstract was complete. J.A. 30 (citing J.A. 22782 (Tr. 204:12–19) (Dr. Lublin testifying that abstracts "have to by design" leave out information describing clinical trials); J.A. 23475 (Tr. 897:1–5) (Dr. Steinman testifying that "an abstract, like a press release, like any kind of announcement, is inherently incomplete," while "a publication and a patent are presumed complete")). Thus, although neither the '405 specification nor Kappos 2006 include the phrase "loading dose," it was not clear error for the district court to find that a skilled artisan would read the specification as not including a loading dose and would read Kappos 2006 as silent on the presence or absence of a loading dose.

Differences between the '405 patent's specification and Kappos 2006 justify the district court's findings that the specification describes the absence of a

loading dose while Kappos 2006 does not anticipate that negative limitation. The specification includes the Prophetic Trial, which the district court found "describes giving a 'daily dosage of 0.5 . . . mg' fingolimod to treat RRMS, started 'initially.'" J.A. 26. The district court found that, "[o]n this record, starting with a daily dose plainly implies that there is no loading dose." J.A. 27. Kappos 2006 consists of two paragraphs describing a planned clinical trial and, with respect to dosing, states only that "[a]pproximately 1.100 patients . . . are being randomised in a 1:1:1 ratio to once-daily fingolimod 1.25 mg, fingolimod 0.5 mg, or placebo, for up to 24 months." J.A. 24723–24. Kappos 2006 nowhere says that the daily fingolimod dosage should be "initially" administered. Thus, differences between Kappos 2006 and the '405 patent justify the district court's conclusions that Kappos 2006 does not anticipate the claims and the '405 specification adequately describes the claims.

The dissent takes umbrage with the district court's finding that the "Prophetic Trial describes giving a 'daily dosage of 0.5 . . . mg' fingolimod to treat RRMS, started 'initially'" because the '405 patent says "[i]nitially, patients receive treatment for 2 to 6 months." Dissent at 6–7; J.A. 26; '405 patent col. 11 ll. 13–14. The dissent would find that the "word 'initially' is not modifying the daily dosage; it is modifying the initial length of treatment in this example." Dissent at 6–7. The dissent, thus, would substitute its own factual findings for those of the district court. But, if the 2–6 month "initial" dose does not differ in any way from the

previously described daily doses, the language, used in context, must exclude a loading dose. As we have already explained, the district court did not clearly err in finding that the "Prophetic Trial describes giving a 'daily dosage of 0.5 . . . mg' fingolimod to treat RRMS, started 'initially.'" J.A. 26. And we are not free to substitute our own factual findings for those of the district court absent clear error because "a district court judge who has presided over, and listened to, the entire proceeding has a comparatively greater opportunity to gain the necessary 'familiarity with specific scientific problems and principles,' . . . than an appeals court judge who must read a written transcript or perhaps just those portions referenced by the parties." *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 319 (2015) (quoting *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 610 (1950)).

The dissent also asserts that, on this record, the term "daily dose" would not convey to a skilled artisan that no loading dose should be used. Dissent at 7–8. But the district court's decision did not rely only on the term "daily dose." Rather, as noted above, the district court found that "*starting* with a daily dose plainly implies that there is no loading dose," as a loading dose is a larger-than-daily dose. J.A. 27 (emphasis added). We need not, and do not, go further than the district court to make findings about the term "daily dose." The dissent's assertion to the contrary and allegation that we "tease[] an entirely new claim limitation out of an entirely common term, relegating the legal determination of a term's meaning to the backseat of an expert's

post-hoc rationalization" is, frankly, baffling. *See* Dissent at 8.

Written description in this case, as in all cases, is a factual issue. In deciding that the district court did not clearly err in finding written description for the negative limitation in the '405 patent, we do not establish a new legal standard that silence is disclosure, as the dissent asserts. Instead, we merely hold that, on this record, the district court did not clearly err in finding that a skilled artisan would read the '405 patent's disclosure to describe the "absent an immediately preceding loading dose" negative limitation.

III. Conclusion

For the foregoing reasons, we affirm the district court's decision.

AFFIRMED

United States Court of Appeals
for the Federal Circuit

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff-Appellee

v.

ACCORD HEALTHCARE, INC., AUROBINDO PHARMA LTD., AUROBINDO PHARMA USA, INC., DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., EMCURE PHARMACEUTICALS LTD., HERITAGE PHARMACEUTICALS INC., GLENMARK PHARMACEUTICALS INC., USA, GLENMARK PHARMACEUTICALS LIMITED, HETERO USA, INC., HETERO LABS LIMITED UNIT-V, HETERO LABS LIMITED, MYLAN PHARMACEUTICALS, INC., PRINSTON PHARMACEUTICAL INC., STRIDES GLOBAL PHARMA PRIVATE LIMITED, STRIDES PHARMA, INC., TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD., ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., APOTEX INC., APOTEX CORP., SUN PHARMACEUTICAL INDUSTRIES, LTD., SUN PHARMACEUTICAL INDUSTRIES INC., SUN PHARMA GLOBAL FZE,

Defendants

HEC PHARM CO., LTD., HEC PHARM USA INC.,

Defendants-Appellants

2021-1070

Appeal from the United States District Court for the District of Delaware in No. 1:18-cv-01043-KAJ, Circuit Judge Kent A. Jordan.

MOORE, *Chief Judge*, dissenting.

The majority dramatically expands a patentee's ability to add, years after filing a patent application, negative claim limitations that have zero support in the written description. By doing so, it contradicts our well-established precedent and nullifies the Patent Office's guidance in the Manual of Patent Examining Procedure (MPEP). I would reverse the district court's finding that there exists written description support as it is inconsistent with our established precedent. Silence is not disclosure.

I

"The hallmark of written description is disclosure." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (en banc). The description in the specification must clearly allow a skilled artisan to recognize that the inventor invented what is claimed. *Id.* The '405 patent contains no written description support for the limitation "absent an immediately preceding loading dose regimen." This negative limitation was added in response to an obviousness rejection during prosecution of the '405 patent's co-pending parent application. J.A. 23892–94. Claim 1:

> 1. A method for reducing or preventing or alleviating relapses in Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, *absent an immediately preceding loading dose regimen.*

There is no disclosure in the specification of preventing a loading dose. Loading doses—whether to be used or not—are never discussed. As the majority concedes, we have long held that silence cannot support a negative limitation; for if the specification is silent there is no evidence that the inventor actually possessed the invention. Maj. at 17 ("Both the MPEP and the dissent are correct in their statement of the law: the 'mere absence of a positive recitation' is not enough, and 'silence alone is insufficient.' "). "Negative claim limitations are adequately supported when the specification *describes a reason to exclude* the relevant limitation," such as by listing the disadvantages of some embodiment. *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1351 (Fed. Cir. 2012). In *Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1356 (Fed. Cir. 2015), we explained that reciting alternative features of the patented invention may also suffice.[1] In *Nike, Inc. v.*

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[1] *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629, 657–59 (E.D. Tex. 2017), consistent with *Inphi*, holds that when a patent discloses many alternatives, the claims are permitted to claim only some and exclude others. The

Adidas AG, we again reiterated that the specification should indicate a reason to exclude. 812 F.3d 1326, 1348 (Fed. Cir. 2016). This law, our law, does not create a heightened standard for negative claim limitations; it simply requires some disclosure to demonstrate that the inventor was not, as in this case, ambivalent about loading doses.[2]

Following our clear precedent, the Patent Office's MPEP provides the following guidance: "The mere absence of a positive recitation is not a basis for an exclusion," i.e., silence alone is insufficient. MPEP § 2173.05(i). That remains true even if it would have been obvious to a skilled artisan to exclude the undisclosed feature. *Rivera v. Int'l Trade Comm'n*, 857 F.3d 1315, 1322 (Fed. Cir. 2017) ("The knowledge of ordinary artisans may be used to inform what is actually in the specification, but not to teach limitations that are not in the specification, even if those limitations would be rendered obvious by the disclosure.").

Nowhere in the patent does it say a loading dose should not be administered. Nowhere does it discuss alternatives (including or not including a loading dose). Nowhere does it give advantages or disadvantages of including a loading dose. Indeed, it provides no

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specification here does not disclose alternatives (some with and some without loading doses).

[2] *In re Bimeda Research & Development Ltd.*, 724 F.3d 1320, 1323–24 (Fed. Cir. 2013), does not help the majority at all. The court simply held that, when the patent repeatedly emphasizes that the invention was "without using antibiotics," a claim which allows some antibiotics lacks written description support. *Id.*

reason to exclude a loading dose. Even Novartis' expert, Dr. Lublin, agreed:

> Q: Nothing in the text of the specification of the '405 patent discloses a rationale for the negative limitation prohibiting an immediately preceding loading dose, correct?
>
> A: I don't believe so.

J.A. 22872–73. And all the experts agreed that loading doses are sometimes given to MS patients. *See* J.A. 22780 (Dr. Lublin explaining that loading doses have been used in trials of MS drugs and with fingolimod in particular); J.A. 22794; J.A. 23347–48 (Dr. Steinman, Novartis' second physician expert, acknowledging that loading doses are used in MS treatments); J.A. 23475 (Dr. Jusko, Novartis' pharmacology expert, testifying that fingolimod was given to transplant patients with a loading dose, and that he "could envision the possibility of starting with a loading dose"). The '405 patent provides nothing to signal to the public that the inventors possessed a treatment excluding a loading dose when a loading dose was a known possibility.

The patent is silent, eerily silent. Consistent with *Santarus, Inphi*, and *Nike*, there needed to be some discussion of loading doses in order to show that the inventors in fact invented this treatment method that is not just ambivalent to, but expressly excludes, a loading dose. This is not a heightened written description requirement; it is simply a written description requirement.

The district court relied on the disclosure's silence to support the negative loading dose limitation, reasoning that silence "would tell a person of skill that loading doses are excluded from the invention." J.A. 26 ¶ 61. We have rejected the notion that a skilled artisan's knowledge can speak for a mute specification. *See Rivera*, 857 F.3d at 1322. Here, the expert that the majority relies upon to supplement a silent disclosure concludes that a loading dose is excluded because the patent is silent on loading doses: "the patent [i]s a document, as a complete document, that should give you all the information you need to carry out the claims, and that information of having a loading dose is not there." Maj. at 19–20 (quoting J.A. 22791). If silence were sufficient then every later-added negative limitation would be supported as long as the patent makes no mention of it. This is a fundamental error of law.

Novartis explained its support for the no-loading-dose limitation as follows:

> Judge Linn: There is nothing in the patent that says treatment begins with the daily dose?
>
> Novartis: Ummm the prophetic example says treatment begins initially and treatment is the 0.5 mg daily dose so if that begins initially it excludes the possibility of a loading dose.
>
> ***
>
> Chief Judge Moore: The patent says "Initially, patients receive treatment for 2 to 6 months,"

> and you believe I should construe that as initially there is no loading dose?
>
> Novartis: Yes, your honor a loading dose is excluded from that treatment.

Oral Argument at 35:30–37:13. The majority claims that the Prophetic Example in the specification describes "start[ing] 'initially' " by "giving a 'daily dose of 0.5 . . . mg.' " Maj. at 7; Maj. at 22 (same). This is a false and inaccurate quotation. The word "initially" does not precede or modify the daily dosage sentence; it follows it three full sentences later. To be clear, the patent does NOT say treatment begins initially with a daily dose. Here is the actual quote:

> 20 patients with relapsing-remitting MS receive said compound at a *daily* dosage of 0.5, 1.25 or 2.5 mg p.o. The general clinical state of the patient is investigated weekly by physical and laboratory examination. Disease state and changes in disease progression are assessed every 2 months by radiological examination (MRI) and physical examination. *Initially*, patients receive treatment for 2 to 6 months. Thereafter, they remain on treatment for as long as their disease does not progress and the drug is satisfactorily tolerated.

'405 patent at 11:8–16. The word "initially" is not some complex, scientific term in need of expert explanation. It is basic English. The word "initially" is not modifying the daily dosage; it is modifying the initial length of

treatment in this example.[3] To the extent that the district court reached a fact finding to the contrary, it is inconsistent with the straight-forward, quite clear language of the patent and therefore clearly erroneous.[4]

Novartis also claims that the use of the term "daily dosage" itself would convey to a skilled artisan that no loading dose should be used. This is not only unsupported by the record; it is contradicted at every turn. First, the claim already said "daily dosage" before the negative limitation was added. It was allowed only after the applicants added the no loading dose limitation. J.A. 23903 (Examiner's rejection in parent application); J.A. 23892–93 (Applicant Response in same); *see also* Novartis Br. 11–12. The applicants explained they added the no-loading-dose limitation "to specify that the [daily dosage] cannot immediately follow a loading dose regiment. Applicants have made these amendments to further distinguish their claims from the disclosure of [the prior art]." J.A. 23892.[5] If daily already meant no loading dose, then there would have been no reason for the claims to recite both a "daily

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[3] I note that even if the Prophetic Example were to be understood as not having included a loading dose that does not mean that loading doses must be prohibited (as the claims now require).

[4] Nothing about this analysis "substitute[s] . . . factual findings for those of the district court." Maj. at 23. Instead, it merely points out how it is *clear error* for the majority, district court, and Novartis to misquote the specification.

[5] Novartis stated during argument that this limitation was "added to *clarify* that the claim does not overlap with [the prior art]." Oral Argument at 21:34–41. This litigation claim cannot be reconciled with their own prosecution statements.

dosage" and the negative loading dose limitation. The same logic applies to the specification, which only mentioned "daily dosage." This prosecution makes clear that neither the applicant nor the examiner believed that the use of the term "daily dosage" alone conveyed the absence of a loading dose.

There is no evidence that daily had a special meaning in the field of pharmacology. Daily is not a complex or complicated term of art that requires expert testimony to explain. The district court construed the claim term "daily dosage of 0.5 mg" to mean "the amount of drug that someone takes in a given day." J.A. 18670. Neither party argued the term excludes a loading dose. *Id.* And for good reason—it has a plain meaning, and the prosecution history shows it does not implicitly exclude a loading dose. Novartis backdoors a claim construction argument, arguing that "experts understood the patent's description of a 'daily dose' as exclusive of a loading dose," Novartis Br. 46, but it and the district court already defined daily dosage otherwise.

Rather than defend Novartis' reliance on the "daily dosage" language, the majority pivots to focus on the district court's statement that "*starting* with a daily dose plainly implies that there is no loading dose." Maj. at 23–24 (quoting J.A. 27). But that statement is just another example of the district court (and now the majority) rewriting the specification with expert testimony. The patent never says "starting with a daily dose," and the district court relied exclusively on expert testimony to support that finding. *See* J.A. 27

(citing J.A. 23344). But "[t]he knowledge of ordinary artisans may . . . not [be used] to teach limitations that are not in the specification[.]" *Rivera*, 857 F.3d at 1322. Novartis, and now the majority, teases an entirely new claim limitation out of an entirely common term, relegating the legal determination of a term's meaning to the backseat of an expert's post-hoc rationalization.

In fact, the district court found that a nearly identical disclosure in the prior art (Kappos 2006, a Novartis-supported study) did not anticipate because it failed to disclose the negative loading dose limitation. Kappos disclosed a study administering 0.5 mg fingolimod to RRMS patients "*once-daily* fingolimod for up to 24 months." J.A. 29–30 ¶ 72; J.A. 24724. The district court found Kappos 2006 did *not* meet the negative loading-dose limitation, reasoning that "[t]he failure to mention a loading dose does not . . . indicate that the dose was not present in the trial, but only that the presence or absence of a loading dose was not mentioned." J.A. 30 ¶ 74. A district court's "internally inconsistent factual findings," like those here, "are, by definition, clearly erroneous." *In re Sentinel Mgmt. Grp., Inc.*, 728 F.3d 660, 670 (7th Cir. 2013); *see also United States v. AT&T, Inc.*, 916 F.3d 1029, 1033 (D.C. Cir. 2019) (citing, e.g., *Anderson v. City of Bessemer, N.C.*, 470 U.S. 564, 575 (1985)) ("A finding may be clearly erroneous when it is illogical or implausible, [or] rests on internally inconsistent reasoning.").

The majority's attempts to distinguish Kappos 2006 from the '405 patent fall flat. Maj. at 21–23. To be sure, Kappos 2006 does not "say[ ] the daily fingolimod

dosage should be 'initially' administered." *Id.* at 22–23. But neither does the '405 patent. The '405 patent uses the word initially to describe the *length of treatment*, not the *dosage*. And it is simply not correct that an issued patent is "presumed to have a complete written description." Maj. at 21. "The presumption of validity includes a presumption the patent complies with" the written description requirement. *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195 (Fed. Cir. 1999). But it does not require presuming an issued patent is "complete," which would mean silence presumptively supports a negative limitation in *every* case. That presumption is contrary to our longstanding precedent, which the majority recognizes (*see* Maj. at 17), and a gross expansion of the presumption of validity.

This specification is ambivalent as to loading doses in a field where, by all expert accounts, loading doses of fingolimod were sometimes used to treat MS. The inventors do not get to claim as their invention something they did not disclose in the patent. There are no fact findings here to defer to—the patent is silent as to loading doses. The district court relied upon that silence: "The absence of an immediately preceding loading dose from the specification, and from the Prophetic Trial, would tell a person of skill that loading doses are excluded from the invention." J.A. 26 ¶ 61. This is not a finding of fact; it is a misunderstanding of the law. An inventor cannot satisfy the written description requirement through silence. And when the majority concludes otherwise, it creates a conflict

with our long-standing, uniformly-applied precedent including *Santarus, Inphi*, and *Nike.* While the negative limitation need not be recited in the specification *in haec verba*, there must be something in the specification that conveys to a skilled artisan that the inventor intended the exclusion: disadvantages, alternatives, inconsistencies, just something. This specification is entirely silent and ambivalent about loading doses. These inventors did not disclose treatment that must exclude a loading dose, and the district court's finding to the contrary is clearly erroneous. After this case, negative limitations are supported by a specification that simply never mentions them.

APPENDIX C

NOTE: This order is nonprecedential.

United States Court of Appeals for the Federal Circuit

January 4, 2022

ERRATA

Appeal No. 21-1070

NOVARTIS PHARMACEUTICALS CORPORATION,
Plaintiff-Appellee

v.

ACCORD HEALTHCARE, INC., AUROBINDO PHARMA LTD., AUROBINDO PHARMA USA, INC., DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., EMCURE PHARMACEUTICALS LTD., HERITAGE PHARMACEUTICALS INC., GLENMARK PHARMACEUTICALS INC., USA, GLENMARK PHARMACEUTICALS LIMITED, HETERO USA, INC., HETERO LABS LIMITED UNIT-V, HETERO LABS LIMITED, MYLAN PHARMACEUTICALS, INC., PRINSTON PHARMACEUTICAL INC., STRIDES GLOBAL PHARMA PRIVATE LIMITED, STRIDES PHARMA, INC., TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD., ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., APOTEX INC., APOTEX CORP., SUN PHARMACEUTICAL

INDUSTRIES, LTD., SUN PHARMACEUTICAL INDUSTRIES INC., SUN PHARMA GLOBAL FZE,
Defendants

HEC PHARM CO., LTD., HEC PHARM USA INC.,
Defendants-Appellants

Decided: January 3, 2022
Precedential opinion

Please make the following change:

Page 2, line 7 (majority opinion): the issuance date of "January 3, 2021" is changed to "January 3, 2022".

APPENDIX D

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ACCORD HEALTHCARE INC., ET AL., Defendants.	C.A. No. 18-1043-KAJ

ORDER, FINAL JUDGMENT, AND INJUNCTION

(Filed Sep. 11, 2020)

WHEREAS, this patent infringement action was brought by Novartis Pharmaceuticals Corporation ("Novartis") alleging, *inter alia*, that Abbreviated New Drug Application ("ANDA") No. 207939, submitted by defendants HEC Pharm Co., Ltd. and HEC Pharm USA Inc. (collectively, "HEC"),[1] infringed claims 1–6 of U.S. Patent No. 9,187,405 (the " '405 Patent"). (*See* D.I. 1.)

WHEREAS, HEC pled defenses and filed declaratory judgment counterclaims against Novartis alleging invalidity and non-infringement of the '405 Patent, (*see* D.I. 134);

[1] Defendant HEC Pharm. Group was previously dismissed from the case. (*See* D.I. 122.)

WHEREAS, Novartis's actions against all other Defendants in this case have been settled and/or stayed;

WHEREAS, the Court held a four-day bench trial from March 2 to 5, 2020;

WHEREAS, the Court issued its Findings of Facts and Conclusions of Law on August 10, 2020 (D.I. 769); and

WHEREAS, the stays against all remaining defendants shall be subject to disposition upon entry of judgment against HEC;

IT IS ORDERED AND ADJUDGED that:

1. Pursuant to Federal Rule of Civil Procedure 54(b), there is no just reason to delay the entry of this Final Judgment against HEC.

2. Final judgment is entered in favor of Novartis and against HEC (1) on Novartis's claims of induced and contributory infringement under 35 U.S.C. § 271(e)(2) of claims 1–6 of the '405 patent by HEC's ANDA No. 207939 and (2) on HEC's defenses and counterclaims of non-infringement and invalidity of claims 1–6 of the '405 patent, and HEC's counterclaims are dismissed with prejudice.

3. Pursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any final approval by the United States Food and Drug Administration of HEC's ANDA No. 207939 shall be a date not earlier than the expiration date of the '405 Patent, including any extensions

and/or additional periods of exclusivity to that date, except to the extent subsequently (a) agreed between Novartis and HEC or (b) ordered or otherwise permitted by this Court or other tribunal. In the event HEC seeks a stay of the effect of the preceding sentence, HEC shall file and serve a motion to stay by no later than 14 calendar days after entry of this order. Any opposition shall be filed and served no later than 14 calendar days thereafter, and any reply shall be filed and served no later than 7 calendar days after any opposition. All motion papers shall comply with the rules for motions in the Local Rules for the District of Delaware, except that page limits shall be limited as follows: opening and responsive briefs are limited to 10 pages and replies to 5 pages.

4. Pursuant to 35 U.S.C. § 271(e)(4)(B), HEC, its affiliates, subsidiaries, and each of their officers, agents, servants, and employees, those acting in privity or in concert with them, and any person or entity to whom HEC transfers ANDA No. 207939, are hereby permanently enjoined from engaging in the commercial manufacture, use, offer for sale, and/or sale in the United States and/or importation into the United States of the fingolimod product that is the subject of HEC's ANDA No. 207939 until the expiration date of the '405 Patent, including any extensions and/or additional periods of exclusivity to that date, except to the extent subsequently (a) agreed between Novartis and HEC or (b) ordered or otherwise permitted by this Court or other tribunal.

5. In the event that a party appeals this Final Judgment, any motion for attorneys' fees and/or costs, including any motion that this case is exceptional under 35 U.S.C. § 285, shall be considered timely if filed and served within 60 days after final disposition of any such appeal, and the responding party shall have 60 days after filing and service to respond.

6. In the event that no party appeals this Final Judgment, any motion for attorneys' fees and/or costs, including any motion that this case is exceptional under 35 U.S.C. § 285, shall be considered timely if filed and served within 60 days after the expiration of the time for filing a notice of appeal under Fed. R. App. P. 3 and 4, and the responding party shall have 60 days after filing and service to respond.

7. In the event Novartis seeks exoneration, release, or other relief from the Preliminary Injunction bond entered in this case (D.I. 632), Novartis shall file any such motion by no later than 14 calendar days after entry of this order. Any opposition shall be filed and served no later than 14 calendar days thereafter, and any reply shall be filed and served no later than 7 calendar days after any opposition. All motion papers shall comply with the rules for motions in the Local Rules for the District of Delaware, except that page limits shall be limited as follows: opening and responsive briefs are limited to 10 pages and replies to 5 pages.

IT IS SO ORDERED this 11th day of September, 2020

/s/ Kent A. Jordan
Honorable Kent A. Jordan,
Third Circuit Judge
Sitting by Designation

Approved as to form and substance:

MCCARTER & ENGLISH, LLP

/s/ Daniel M. Silver
Michael P. Kelly (#2295)
Daniel M. Silver (#4758)
Alexandra M. Joyce (#6423)
Renaissance Centre
405 N. King Street, 8th Floor
Wilmington, DE 19801
(302) 984-6300
mkelly@mccarter.com
dsilver@mccarter.com
ajoyce@mccarter.com

STAMOULIS & WEINBLATT, LLP

/s/ Stamatios Stamoulis
Stamatios Stamoulis (#4606)
Richard C. Weinblatt (#5080)
800 N. West St., 3rd Floor
Wilmington, DE 19801
(302) 999-1540
stamoulis@swdelaw.com
weinblatt@swdelaw.com

Mieke Malmberg
SKIERMONT DERBY LLP
800 Wilshire Blvd., Ste. 1450
Los Angeles, CA 90017
(213) 788-4502
mmalmberg@skiermontderby.com

Jane M. Love, Ph.D.
Robert W. Trenchard
Paul E. Torchia
Laura Corbin
GIBSON, DUNN & CRUTCHER LLP
200 Park Avenue
New York, NY 10166
(212) 351-4000
jlove@gibsondunn.com
rtrenchard@gibsondunn.com
ptorchia@gibsondunn.com
lcorbin@gibsondunn.com

Andrew P. Blythe
GIBSON, DUNN & CRUTCHER LLP
333 South Grand Avenue
Los Angeles, CA 90071
(213) 229-7000
ablythe@gibsondunn.com

Christine L. Ranney
GIBSON, DUNN & CRUTCHER LLP
1801 California St.
Denver, CO 80202
(303) 298-5700
cranney@gibsondunn.com

Attorneys for Novartis Pharmaceuticals Corporation

Paul Skiermont
Sarah Spires
Steven J. Udick
SKIERMONT DERBY LLP
1601 Elm Street, Suite 4400
Dallas, TX 75201
(214) 978-6600
pskiermont@skiermontderby.com
sspires@skiermontderby.com
sudick@skiermontderby.com

Attorneys for HEC Pharm Co. & HEC Pharm USA Inc.

APPENDIX E

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ACCORD HEALTHCARE INC., et al., Defendants.	)	Civil Action No. 18-1043-KAJ

ORDER

(Filed Aug. 17, 2020)

In accordance with the Court's August 10, 2020 Order (D.I. 770), the Clerk's Office is hereby directed to unseal the Findings of Fact and Conclusions of Law of August 10, 2020 (D.I. 769).

/s/ Kent A. Jordan
Kent A. Jordan
Circuit Judge sitting by designation

DATE: August 17, 2020
Wilmington, Delaware

APPENDIX F

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ACCORD HEALTHCARE INC., et al., Defendants.	)	Civil Action No. 18-1043-KAJ **FILED UNDER SEAL**

POST-TRIAL FINDINGS OF FACT AND CONCLUSIONS OF LAW

(Filed Aug. 10, 2020)

I. INTRODUCTION

Plaintiff Novartis Pharmaceuticals Corporation ("Novartis") owns Patent No. US 9,187,405 B2 ("the '405 Patent" or "the Patent"), which claims methods to treat Relapsing-Remitting multiple sclerosis ("RRMS") using a compound called "fingolimod," at a daily dosage of 0.5 mg, absent an immediately preceding loading dose. Novartis sells fingolimod under the brand name Gilenya, which the FDA approved in 2010. Defendants HEC Pharm Co., Ltd., HEC Pharm Group, and HEC Pharm USA Inc. (collectively, "HEC") submitted an Abbreviated New Drug Application ("ANDA") to the FDA, seeking approval to make fingolimod 0.5 mg capsules,

a generic copy of Novartis's Gilenya product, prior to the expiration of the '405 Patent.[1]

Novartis then brought this suit, alleging that HEC's ANDA infringes the '405 Patent. HEC, of course, disputes that. It claims that its label does not instruct physicians to omit a loading dose from the dosing regimen, so it is not practicing one of the elements of the patent claims in suit.

HEC also brought a counterclaim that the '405 Patent is invalid for lack of written description and anticipation. As to written description, HEC claims that the Patent has no written description for the negative limitation "absent an immediately preceding loading dose" or for the claimed 0.5mg daily dose. And concerning anticipation, HEC argues that the '405 Patent is anticipated by an abstract published in the Journal of Neurology and presented at the European Neurologic Society Meeting in 2006. Novartis responds that the Patent specification provides the necessary written description and that the abstract does not anticipate because it is not prior art, does not disclose the claimed invention, and is not enabled.

The parties presented their cases during a four-day bench trial from March 2-5, 2020. As explained below, I conclude that HEC is liable for contributory and induced infringement because the label for its generic version of Gilenya instructs physicians to perform each limitation in the asserted claims of the Patent. I

[1] All other defendants in this case have settled with Novartis.

further conclude that the Patent is not invalid. The Patent contains an adequate written description, and it was not anticipated by the abstract. The following are my findings of fact and conclusions of law.

II. FINDINGS OF FACT

A. The Parties and the Patent

1. Plaintiff Novartis is a corporation organized and existing under the laws of Delaware, having a principal place of business at 1 Health Plz, East Hanover, New Jersey 07936. (D.I. 715, Pretrial Order ("PTO") Ex. 1 ¶ 1.)

2. Defendant HEC Pharm Co., Ltd. is a corporation organized and existing under the laws of China, having a principal place of business at Binjiang Road 62, Yidu, Yichang, 443300, Hubei, China. Defendant HEC Pharm USA Inc. is a corporation organized and existing under the laws of New Jersey, having a principal place of business at 116 Village Blvd, Suite 200, Princeton, NJ 08540. (*Id.* ¶¶ 2-3.) As noted in the Introduction, *supra*, HEC Pharm Co., Ltd., HEC Pharm USA Inc., and HEC Pharm Group are referred to collectively herein as "HEC."

3. Novartis owns the '405 Patent, which claims methods to treat RRMS with 0.5 mg of fingolimod daily absent an immediately preceding loading dose. (JTX-001.) The claims of the '405 Patent, all of which are asserted in this case, are as follows:

    1. A method for reducing or preventing or alleviating relapses in Relapsing-Remitting multiple sclerosis in a subject in need

thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl) ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

2. The method according to claim 1 wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered.

3. A method for treating Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl) ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

4. The method according to claim 3 wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered.

5. A method for slowing progression of Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

6. The method according to claim 5 wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered. (JTX-001 at 12:48-13:10.)

4. The specification describes an example of the claimed dosing regimen in a prophetic human clinical trial ("the Prophetic Trial"), where RRMS patients receive fingolimod "at a daily dosage of 0.5" mg for at least two to six months. (*Id.* at 11:8-14.) There is no mention of a loading dose. (*Id.*) A prophetic trial is a study that is described on paper but not actually performed. (Tr. at 734:1-736:2.) Because FDA-approved clinical trials take a long time to perform, prophetic trials are sometimes used in patent applications to explain "if the drug were effective [in humans at a dose observed to be effective in animals], how you administer it, at what dose, and how you would follow the patient on that dose to understand whether clinical benefit was being achieved." (*Id.* at 735:2-6.)

5. The specification also describes the results of an Experimental Autoimmune Encephalomyelitis experiment ("EAE" experiment). (JTX-001 at 10:32-11:2.) In the EAE experiment, disease that mimics RRMS is induced in laboratory animals called Lewis rats, with "an acute disease within 11 days, followed by an almost complete remission around day 16 and a relapse at around days 26." (*Id.* at 10:35-39.) The specification says that 0.3 mg/kg of fingolimod, given once a week, "completely inhibits the relapse phases[.]" (*Id.* at 10:62-11:2.)

6. Novartis sells fingolimod under the brand name Gilenya, which the FDA approved in 2010. Fingolimod hydrochloride is Gilenya's sole active ingredient, at a recommended dose of 0.5 mg daily administered orally in a capsule. (D.I. 715, PTO Ex. 1 ¶ 15.)

7. HEC submitted ANDA No. 207939 to the FDA under the provisions of 21 U.S.C. § 355(j), seeking approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of Fingolimod 0.5 mg capsules, a generic copy of Novartis's Gilenya product, prior to the expiration of the '405 Patent. (*Id.* ¶ 17.)

8. HEC's proposed prescribing information states in the "Dosage and Administration" section of the proposed label submitted with HEC's ANDA that "[i]n adults, the recommended dosage of fingolimod capsule is 0.5 mg orally once-daily." HEC's proposed prescribing information states in the "Indications and Usage" section that "[f]ingolimod capsules are indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 18 years of age and older." (*Id.* ¶¶ 19-20.)

9. Chief Judge Leonard P. Stark presided over this case before it was reassigned to me. He adopted a definition of a person of ordinary skill in the art ("POSA") which is "'a multi-disciplinary research team' that includes '1) a Ph.D. with expertise in the area of neurology and/or an M.D. having several years of clinical experience treating multiple sclerosis patients, and who would be knowledgeable about the multiple sclerosis literature,' and '2) a pharmacologist with experience in drug development.'" (*Id.* ¶ 33.)

10. He also construed the claim preambles ("A method for reducing or preventing or alleviating relapses

in Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising . . . " (Claim 1); "A method for treating Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising . . . " (Claim 3); and "A method for slowing progression of Relapsing Remitting multiple sclerosis in a subject in need thereof, comprising . . . " (Claim 5)) to be a limiting statement of purpose. (D.I. 561 at 5.)

11. He construed the term "daily dosage of 0.5 mg" as the amount of drug that someone takes in a given day. (*Id.* at 9.)

12. I have reviewed those conclusions and fully adopt them here.

B. The Witnesses

1. Dr. Fred Lublin, Ph.D.

13. Dr. Fred Lublin, testifying for Novartis, is a neurologist specializing in MS at the Mount Sinai Medical Center in New York. (Tr. at 107:23-108:7.) Dr. Lublin has been an MS physician for over 40 years, has treated several thousand patients during that time, and continues to treat numerous patients. (*Id.* at 108:18-109:1.) He has published over 200 peer-reviewed publications, the vast majority of which relate to MS or animal models of that disease. (*Id.* at 109:2-13.) Dr. Lublin has been involved in many MS clinical trials for various MS medications. (*Id.* at 110:17-24.)

14. Dr. Lublin was involved in the clinical trials for fingolimod. (*Id.* at 112:13-15.) He was a member of the data safety monitoring board for the Phase I

trial and a member of the advisory committee for the Phase III protocols.[2] (*Id.* at 112:16-20.) He spent approximately 18 years working on the fingolimod clinical trial. (*Id.* at 112:21-23.)

15. At trial, Dr. Lublin was received as an "expert medical doctor specializing in MS and the design [and] execution [of] clinical trials." (*Id.* at 112:24-113:5.)

2. Peter Hiestand (via deposition)

16. Peter Hiestand is one of the named inventors, along with Christian Schnell, on the '405 Patent. (*Id.* at 314:6-15.) Hiestand and Schnell collaborated on the EAE experiment described in the Patent. (*Id.* at 315:3-6, 315:21-316:7.)

17. They "were the first ones to provide proof that the compound will work at 0.5 mg, which, . . . was not known at the time to the persons arranging Phase III trials." (*Id.* at 332:13-17.) Hiestand and Schnell translated the low effective EAE doses they

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[2] Clinical trials are conducted in phases. A Phase I trial involves a small number of people and is studied over a short period of time to test safety and dosing. (Tr. 123:10-15.) A Phase II trial "is called a proof-of-concept study." (*Id.* at 123:23-25.) It involves more participants and lasts longer than a Phase I trial. (*Id.* at 124:1-4.) The researchers in Phase II are still assessing safety and dosing but are also assessing whether a drug may be effective. (*Id.* at 123:25-124:7.) Phase III trials "are called pivotal trials. They involve larger numbers of patients, usually over a thousand; longer periods time. . . . They have to have a clinical endpoint as the primary outcome measure." (*Id.* at 128:19-129:4.) "[I]f you succeed in Phase III, you usually can take that data to someone like the FDA to try and license a drug." (*Id.* at 129:5-7.)

observed to the lower human dose of 0.5 mg through a proportionality analysis. (*Id.* at 319:9-321:18.)

3. Christian Schnell (via deposition)

18. Christian Schnell is one of the named inventors on '405 Patent. (*Id.* at 338:4-7.) He was involved in the EAE experiments that underlie the Patent. (*Id.* at 339:1-341:4.)

4. Peter Waibel (via deposition)

19. Peter J. Waibel is in-house legal counsel for Novartis and was deposed pursuant to Federal Rule of Civil Procedure 30(b)(6) as a designated witness for Novartis. (*Id.* at 353:17-354:1.)

5. Dr. Robert Fujinami, Ph.D.

20. Dr. Robert Fujinami, testifying for HEC, is a Professor in the Department of Pathology, the Vice Dean for Faculty and Academic Affairs for the University of Utah School of Medicine and is the Assistant Vice President for Academic Affairs for University of Utah Health. (*Id.* at 378:2-10.) Dr. Fujinami obtained his Ph.D. from Northwestern University and then received post-doctoral training at the Scripps Research Institute. (*Id.* at 378:25-379:9.)

21. Dr. Fujinami's primary field of research is in EAE and related immunological mechanisms that affect initiation, exacerbations, or remissions in preclinical animal models for multiple sclerosis. (*Id.*

at 378:11-19.) He has experience conducting EAE experiments using Lewis rats and other animal models. (*Id.* at 379:19-380:2.)

22. At trial, Dr. Fujinami was received as an expert, as a Ph.D. with expertise in the area of neurology. (*Id.* at 382:2-8, 383:4-9.)

6. Dr. Peter Calabresi, M.D. (via deposition)

23. Dr. Peter Calabresi is an MS physician, researcher, and professor of neurology at Johns Hopkins. (*Id.* at 423:25-424:19.) He regularly treats MS patients. (*Id.* at 424:20-425:13.) He has been a principal investigator on several multiple sclerosis clinical trials. (*Id.* at 425:14-427:16.) He was the principal investigator for the fingolimod U.S. Phase III trial called "FREEDOMS II." (*Id.*) He was also on the "FREEDOMS I" steering committee, and assisted with study design, including dose selection. (*Id.* at 428:4-429:10.)

24. Dr. Calabresi explained that clinical investigators "enter into a clinical trial with . . . equipoise, where you don't really know in the beginning what the answer is going to be, and that's the reason for doing the clinical trial." (*Id.* at 428:16-429:10.) Phase III clinical trials, "or some arms" thereof, sometimes fail (*id.* 429:11-25), and the Phase III fingolimod investigators entered into that phase with "equipoise" about the 0.5 mg dose (*id.* at 437:16-22).

7. Dr. Radojka Savic, Ph.D.

25. Dr. Radojka Savic, testifying for HEC, is an Associate Professor of Bioengineering & Therapeutic Sciences in the School of Pharmacy and an Associate Professor of Pulmonary and Critical Care in the Department of Medicine at the University of California, San Francisco. (*Id.* at 466:16-467:1.) Dr. Savic obtained her Ph.D. in Pharmacometrics from the School of Pharmacy at Uppsala University in Sweden. (*Id.* at 463:24-464:4.) After obtaining her Ph.D., Dr. Savic did post-doctoral training in biostatistics and pharmacometrics at the French Institute for Health, INSERM in Paris, France and clinical pharmacology at the School of Medicine at Stanford University. (*Id.* at 464:23-465:9.) At the same time, Dr. Savic maintained her status as a researcher in pharmacometrics at Uppsala University, where she was responsible for the entire program of modeling disease progression and PK/PD relationships in several large multiple sclerosis clinical studies for the multiple sclerosis drug Cladribine. (*Id.* at 465:10-21.)

26. At trial, Dr. Savic was received as an expert in clinical pharmacology, including developing dosing regimens between animal and human models, and in clinical trials. (*Id.* at 471:22-472:3.)

8. Dr. Paul Hoffman, M.D.

27. Dr. Paul Hoffman, testifying for HEC, is a senior scientist in the Department of Neurology at the University of Florida's College of Medicine and at University of Florida Health, the clinical arm of the medical school. (*Id.* at 516:15-21.) Prior to that,

Dr. Hoffman worked in the Department of Veteran's Affairs for 35 years, retiring in 2015. (*Id.* at 520:12-17.) Dr. Hoffman's experience includes being a researcher in EAE, reviewing clinical trials, and having over 40 years of experience treating multiple sclerosis patients. (*Id.* at 516:15-522:3; 532:12-533:13.)

28. At trial, Dr. Hoffman was received as an expert medical doctor with particular expertise in the treatment of multiple sclerosis. (*Id.* at 525:9-526:3.)

9. Dr. Shreeram Aradhye (via deposition)

29. Dr. Shreeram Aradhye was, at the time of his deposition, the Chief Medical Officer of Novartis and, during 2003 to 2005, he was the medical lead on the first Phase III trial of fingolimod in transplant patients and the Phase III RRMS trial of fingolimod. (*Id.* at 646:16-22.)

10. Dr. Lawrence Steinman, M.D.

30. Dr. Lawrence Steinman, testifying for Novartis, is an MS physician and researcher, and a Professor of Neurology at Stanford University. (*Id.* at 684:2-8.) Dr. Steinman earned his medical degree from Harvard University in 1973, and subsequently studied under the inventor of the MS drug Copaxone®. (*Id.* at 686:3-12.) Dr. Steinman has treated over 4,000 MS patients, and has prescribed Gilenya many times. (*Id.* at 684:11-21.) He leads a laboratory at Stanford (*id.* at 685:3-5), the institution where he has been conducting MS drug

research since 1975 (*id.* at 686:13-15). Research in Dr. Steinman's laboratory led to the development of an FDA-approved treatment for MS marketed as Tysabri® (natalizumab). (*Id.* at 686:16-21.)

31. Dr. Steinman also has extensive experience with the EAE model: he has conducted approximately 1,000 EAE experiments over the last 45 years (*id.* at 693:10-693:21), and has used both acute and relapsing EAE models (*id.* at 693:22-694:4). Dr. Steinman has published over 500 peer-reviewed publication related to MS or EAE (*id.* at 685:6-12) and is the named inventor on approximately 50 patents (*id.* at 687:15-18).

32. Dr. Steinman has been involved with MS clinical trials, serving in a variety of roles, including as principal investigator and as a member of data safety monitoring boards and advisory boards. (*Id.* at 686:22-687:6.) He has advised companies on the design of clinical trials since the 1980s. (*Id.* at 687:7-14.)

33. At trial, Dr. Steinman was received as an "expert medical doctor with expertise in multiple sclerosis and drug development . . . including clinical trials." (*Id.* at 688:17-689:1.)

11. Dr. William Jusko, Ph.D.

34. Dr. William Jusko, testifying for Novartis, is a distinguished professor of pharmaceutical sciences at the University of Buffalo. Dr. Jusko specializes in pharmacology, and focuses on pharmacokinetics and pharmacodynamics, in particular with respect to immunosuppressants. (*Id.* at 845:12-846:14.)

Dr. Jusko has published over 600 publications in peer-reviewed journals, and has been the editor-in-chief of the primary journal in his field, the Journal of Pharmacokinetics and Pharmacodynamics. (*Id.* at 846:15-847:1.) He has also received prestigious awards in the field of pharmacology. (*Id.* at 847:2-13.)

35. Dr. Jusko's laboratory has conducted pharmacokinetic and pharmacodynamics modeling and analyses for pharmaceutical companies developing immunosuppressant drugs, including for Novartis on fingolimod. (*Id.* at 848:8-24.) Dr. Jusko's studies on fingolimod involved developing complex models for fingolimod in monkeys and rats. (*Id.* at 849:7-850:22.)

36. At trial, Dr. Jusko was received as an expert in pharmacology. (*Id.* at 852:10-17.)

C. Infringement

37. HEC's ANDA included a certification that the '405 Patent is invalid, unenforceable, and/or will not be infringed by HEC's generic fingolimod product. (D.I. 715, PTO Ex. 1 ¶ 21.)

38. HEC's proposed label is materially identical to the label for Gilenya. (PTX-310; Tr. 221:8-22.)

39. HEC's proposed label instructs doctors to perform the '405 Patent's claimed methods for the purposes stated in the preambles of the claims. Those purposes are in Sections 1 and 14 of HEC's proposed label. (Tr. 223:3-225:22.)

40. With respect to the preambles of claims 1 and 5 of the Patent, HEC's product is, according to the proposed label, "indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include . . . relapsing-remitting disease[.]" (PTX-310.0005; Tr. 224:3-15.) The label also describes clinical trials showing the 0.5 mg dose reduced annualized relapse rates and slowed disability progression. (PTX-310.0027-29; Tr. 224:16-225:15, 642:17-643:10.) Reducing relapses and slowing progression are the only two clinical benefits described in HEC's proposed label. (Tr. 224:16-225:2, 642:17-643:16.) The label describes those benefits when summarizing the Phase III clinical trials for RRMS. (*Id.*) Dr. Hoffman testified that he prescribes Gilenya to patients solely for the purposes described in the label's clinical trial section. (*Id.* 643:17-23.)

41. With respect to the preamble of claim 3, again, HEC's ANDA product is, according to the proposed label, "for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include . . . relapsing remitting disease[.]" (PTX-310.0005.)

42. The Patent's claims all require the administration of 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, which is the chemical name for fingolimod. (JTX-001, col. 12-13.) Section 11 of HEC's proposed label instructs that doctors are administering and patients are taking the drug compound fingolimod hydrochloride, and that is as claimed in the '405 Patent. (PTX-310.0020.)

43. The claims require "orally administering . . . [fingolimod] . . . at a daily dosage of 0.5 mg." (JTX-001,

col. 12-13.) HEC's proposed label instructs that "the recommended dosage . . . is 0.5 mg orally once daily[.]" (PTX-310.0006; Tr. 227:2-230:7.) That is the only dose the label recommends. (Tr. 640:14-20.) Any other dose would be off-label. (*Id.* 229:17-230:4.) Other ANDA documents from HEC show that only 0.5 mg – and no more – is the recommended dose. (PTX-273.0001; Tr. 228:6-22.)

44. A loading dose is a "greater-than-normal dose that you usually use at the start of a therapy to . . . jump-start the levels [of a drug] in the body." (Tr. 201:13-16.) HEC's proposed label does not mention a loading dose. (*Id.* at 641:16-22.)

45. Nothing in HEC's proposed label says to prescribe anything more or less than 0.5 mg, and the label provides a caution that there is "a greater incidence of adverse reactions without additional benefit" for doses over 0.5 mg. (PTX-310.0006.)

46. Dr. Hoffman agreed that it would be very unusual to administer a loading dose with fingolimod for an off-label use. (Tr. 547:12-549:2.)

47. Dr. Lublin has prescribed Gilenya to hundreds of patients and has never given Gilenya with a loading dose. (*Id.* at 220:15-18, 230:5-7.)

48. Dr. Hoffman testified that the only clinical benefits for HEC's generic version of Gilenya would be those identified in the clinical trial section of the proposed label. (*Id.* at 642:17-643:23.) Those trials used a dose of 0.5 mg daily, without a loading dose, solely in RRMS patients. (*Id.* at 130:7-22; PTX-310.0027.)

D. Invalidity

1. Written Description

49. A person of skill in the art would understand that the Patent describes a daily dosage of 0.5 mg of fingolimod without a preceding loading dose. A person of skill would understand that the Prophetic Trial in the Patent assumes that the daily dosage of 0.5 mg is an effective treatment, and that the first dose listed in the example is the 0.5 mg daily dose. (Tr. 753:22-754:21.) The Prophetic Trial describes how a person of skill would investigate clinical benefit in patients receiving treatment, i.e. the daily 0.5 mg dose, by seeing the patient, doing neurologic exams, and following the disease with, for instance, magnetic resonance imaging. (*Id.* at 754:22-755:22.) The Prophetic Trial describes the methods persons of skill would use to keep track of patients receiving treatment. (*Id.* at 755:23-756:15.)

50. A person of skill would understand the Prophetic Trial to disclose a method of treatment because it specifies that the purpose of the daily dose is treatment and describes how a person of skill would follow a patient for that treatment. (*Id.* at 753:22-754:15, 804:1-805:10; 863:22-864:18.) Dr. Lublin explained that the Prophetic Trial discloses a treatment purpose because subjects "initially . . . received treatment for two to six months" and then "remain on treatment for as long as their disease does not progress[.]" (JTX-001 11:13-14; Tr. at 233:23-235:5.) There is no placebo group. (Tr. at 235:1-5.)

51. Dr. Lublin explained that while the Prophetic Trial described in the Patent specification was not actually conducted, it provides anticipated results from treatment. (*Id.* at 242:22-243:20.) While the Prophetic Trial would be insufficient for "purposes of the FDA," (*id.* at 267:10-13), patents are viewed from "the purview of a person of ordinary skill" (*id.* at 235:13-235:18), and can be valid and enforceable according to the terms of title 35 of the United States Code, even if other regulatory requirements may exist for approval of the drug covered by the patent in question.

52. Read as a whole, the Patent tells a person of ordinary skill in the art that the invention is about treating RRMS. (*Id.* at 858:20-861:2.) The title indicates that it speaks of a treatment for RRMS. (*Id.* at 860:5-8.) The abstract also mentions that the drug could be used to treat conditions such as multiple sclerosis. (*Id.* at 860:11-13, 20.) Dr. Hoffman agreed that the title and specification of the '405 Patent tell persons of ordinary skill in the art that the invention is about using SIP receptor modulators, including fingolimod, for treating RRMS. (*Id.* at 597:2-10, 619:16-620:6.)

53. The two examples, animal and human, are "complementary" when read together in the context of the entire Patent. (*Id.* at 864:19-24.) Dr. Lublin testified that the Prophetic Trial shows a treatment purpose because, "when you read the patent, . . . in the animal experiment they said we've got it; a lower dose of fingolimod will work. They . . . make the conversion to human dosing, and then they show this clinical trial and that they're

treating it. That's how I read the patent." (*Id.* at 235:19-236:8.)

54. A person of skill would understand that the inventors used a relapsing EAE model. The section of the '405 Patent reporting the experimental results is "In Vivo: Relapsing Experimental Autoimmune Encephalomyelitis (EAE)." (JTX-001.0007 at 10:32-33.) Dr. Hoffman agrees that a person of skill would understand the EAE example to describe a relapsing model, not an acute model. (Tr. 625:19-626:4, 627:15-629:10.) A person of skill would understand the inhibition of relapses could be achieved by any of the dosing schedules described in the EAE example, including the 0.3 mg/kg per week dose. (*Id.* at 629:19-630:16.)

55. A person of skill would understand that the Lewis rat animal model is a good model for relapsing EAE. (*Id.* at 838:9-840:19; *see also* 324:23-325:15.) A person of skill would also understand that EAE was the dominant model for studying MS treatments, and that results in EAE were reasonably correlated to results in humans. (*Id.* at 776: 10-13, 639:10-12; PTX-095.001.)

56. The EAE experimental results set forth in the Patent report an effective dose of 0.3 mg/kg weekly. (JTX-001 at 11:2.) According to Dr. Steinman, a person of skill in the art would have converted the 0.3 mg/kg weekly dose to 0.042 mg/kg daily, in order to compare the daily dose with the lowest known effective daily dose. (Tr. at 747:6-748:19.) Dr. Jusko explained that dividing by 7 to go from a weekly to a daily dose is appropriate because fingolimod has a very long half-life, distributes

extensively, and stays in brain tissue for a long time. (*Id.* at 865:12-24, 904:2-904:18.) The method for equalizing exposure between single and multiple doses is well understood and straightforward since the dynamics of lymphocyte suppression were known to be slow. (*Id.* at 866:18-867:4.)

57. According to Dr. Jusko, when reading the EAE experimental results reported in the Patent, a person of skill would immediately recognize that 0.3 mg/kg weekly (0.042 mg/kg daily) in rats is lower than the lowest known effective dose in the prior art (0.1 mg/kg daily). (*Id.* at 862:25-863:21.) It is approximately 60% lower. (Id. at 865:23-24.)

58. A person of skill would understand that the EAE results in the '405 Patent therefore demonstrate that a proportionally lower dose (again, roughly 60% lower) could be effective in humans. (*Id.* at 865:4-867:4, 902:17-907:8.) It was understood from the results of the Phase II trial of fingolimod in patients with RRMS that the lowest known effective dose in humans was 1.25 mg daily. (*Id.* at 706:7-17, 114:17-23.) A 60% lower dose is the 0.5 mg dose described in the Patent. (*Id.*) According to Dr. Jusko, "[w]ith the extensive studies done in the animal model, the appreciable information of some of the pharmacokinetics and some of the pharmacodynamics of humans, the two systems [– animal and human –] were highly in agreement." (*Id.* at 866:10-14.)

59. Dr. Steinman agrees that a person of ordinary skill in the art would understand that the inventors translated the lowest dose that had ever been seen as effective from their EAE experiment (0.3 mg/kg

once per week) to the 0.5 dose. (*Id.* at 778:25-779:14.) The Prophetic Trial would confirm to a person of skill that the inventors did a translation from their EAE experiments to the 0.5 mg daily dose in humans, as exemplified in the Patent. (*Id.* at 865:25-866:9.) It appears that the inventors chose the lowest effective dose, which is the once-weekly regimen, for illustration in the Prophetic Trial. (*Id.* at 257:25-258:10.)

60. A person of skill would understand that the inventors were in possession of the claimed method, based on their innovative EAE experiments, understanding of the mechanism of action, using a well-established model, and the correlation to humans due to "extensive studies done with fingolimod between animals and humans." (*Id.* at 870:20-871:3.)

61. There was no recitation of a loading dose in the specification. (*Id.* at 766:16-767:2.) The Prophetic Trial describes the dosing regimen (dosage, frequency, and length) and does not involve a loading dose. (*Id.* at 214:10-215:11.) The absence of an immediately preceding loading dose from the specification, and from the Prophetic Trial, would tell a person of skill that loading doses are excluded from the invention.

62. The Prophetic Trial describes giving a "daily dosage of 0.5 . . . mg" fingolimod to treat RRMS, started "initially." (JTX-001 at 11:8-13.) The Prophetic Trial tells a person of skill that on day 1, treatment begins with a daily dose of 0.5 mg, not a loading dose. (Tr. at 765:5-766:2.) If a loading dose were directed, the Patent would say that a

loading dose should be administered "initially." (*Id.* at 756:16-757:8 ("[I]t was zero out of two places where they . . . necessarily would have put it in."); *id.* at 863:22-864:18 ("They specified [an] initial regimen that does not include a loading dose.").)

63. A loading dose is necessarily a higher-than-daily dose. (*Id.* at 766:4-766:6.) On this record, starting with a daily dose plainly implies that there is no loading dose. (*Id.* at 766:7-15.) Dr. Hoffman agreed that a loading dose is usually given "as the first dose[.]" (*Id.* at 547:12-18.)

64. The EAE example discloses a dosing regimen which does not involve a loading dose. (*Id.* at 767:3-5; 215:16-21.) Dr. Hoffman, testifying for HEC, agreed. (*Id.* at 631:18-22.)

65. The Patent describes alternative dosing regimens, like "intermittent dosing," but does not describe loading doses. (*Id.* at 617:12-617:23.)

66. A person of skill in 2006 would not expect a loading dose to be used to treat RRMS with fingolimod. (*Id.* at 548:2-549:2, 551:6-12.)

2. <u>Anticipation</u>

67. The abstract published in the Journal of Neurology and presented at the European Neurologic Society Meeting in 2006, *Design of a randomized, placebo-controlled study of oral fingolimod (FFTY720) in relapsing-remitting multiple sclerosis* ("Kappos 2006"), and dated Mary 27-31, 2006, does not anticipate the Patent. (DTX-047; Tr. 186:2-9.) Kappos 2006 announces an upcoming

Phase III trial of 1.25 mg and 0.5 mg doses of fingolimod daily compared to a placebo. (DTX-009.)

68. First, there is insufficient evidence to establish Kappos 2006 as prior art, as it has not been shown to have been available before June 27, 2006.[3] A copy of Kappos 2006 with a declaration from an employee from the British Library was offered but not admitted into evidence. The declaration is inadmissible hearsay and, in any event, is internally inconsistent regarding the location and availability of the document. (Tr. at 372:15-16; DTX-009.) The library stamp on the cover of the journal refers to a "Document Supply Centre," while the declaration refers instead to a "reading room." (Tr. at 367:23-370:21; DTX-009.)

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[3] The parties agree that June 2006 is the relevant time period for when prior art had to be publicly available in order to anticipate the patent. (*Compare* Tr. 43:25-44:2, 44:13-14, *with* Tr. 984:2-7, *and* 813:6-8.) The inventors filed a patent application in Great Britain on June 27, 2006. A Patent Cooperation Treaty application was filed on June 25, 2007. That application was translated and filed in the United States Patent and Trademark Office as U.S. Serial No. 12/303,765 (the "'765 Application"). The '405 Patent is a division of U.S. Application No. 13/149,468, filed on May 31, 2011, which is a continuation of the '765 Application. (D.I. 715, PTO Ex. 1 ¶ 13.) Based on the pre-America Invents Act 35 U.S.C. § 102(b), HEC says that publications are prior art only if published more than a year before the United States filing, so June 25, 2006. (D.I. 748 at 3.) Novartis says that the priority date, and thus the relevant date to determine if a document is prior art, is when the patent was filed in Great Britain – June 27, 2006. (D.I. 758 at 28.) For purposes of analysis, I can accept either June 25 or June 27, 2006 as the relevant date. Despite HEC advocating for June 25, it appears that June 27 is the more favorable date for HEC.

69. The declarant, Rupert Lee, was not present at trial and not available for deposition. His declaration states that his "knowledge of the records and record keeping practices and procedures of the Library [] relies to some extent on information collated by a third party." (DTX-9.00001; *see also* Tr. at 369:20-370:6.) Mr. Lee admits that he was not involved in the cataloging process for Kappos 2006, and his declaration was made 12 years after the event. (DTX-9.00001-00002.)

70. Mr. Lee does not provide any information on the procedures for cataloging, indexing, or shelving. For instance, there is no information about: (1) the cataloging process; (2) what happens to a reference once it is cataloged; (3) how the reference gets to a publicly accessible location; (4) who was responsible for carrying out such procedures; (5) how long such procedures would have taken; (6) how the reference would have been identified or indexed in a reading room; (7) how the existence of the reference would have been made known to the public; (8) how an interested person would search for the reference. (DTX-009.)

71. No evidence was admitted that shows that Kappos 2006 was publicly accessible prior to June 27, 2006. Although witnesses testified that it is typical that such abstracts are printed in advance of the meeting and in conjunction with a presentation at the meeting, there was no testimony verifying that this abstract was actually publicly available or

that it accompanied a presentation.[4] (Tr. at 441:2-442:8; 672:9-673:5.)

72. Kappos 2006 was separately admitted into evidence, without the British Library declaration, as DTX-047. The abstract describes a "study of oral fingolimod (FTY720) in relapsing-remitting multiple sclerosis[.]" (DTX-47.00001-00002.) It suggests three test groups, with dosing levels at 1.25 mg, 0.5 mg, and placebo, in a "randomized, double-blind" study. (DTX-47.00002-00003.)

73. Kappos 2006 does not describe a treatment for RRMS, but rather articulates a test or drug trial. (Tr. at 240:21-23.) To a person of ordinary skill in the art, "[t]esting is not treating." (*Id.* at 175:25-176:1.) The abstract offers no evidence of effectiveness, which a person of skill would look for as an indication of a treatment purpose. (*Id.* at 176:24-177:9.) The inclusion of a placebo group, which involves no treatment of RRMS, further demonstrates that the abstract describes a trial with unknown results. (*Id.* at 176:24-177:9; 895:11-896:5.)

74. Kappos 2006 does not mention a loading dose. (*Id.* at 674:9-11; 894:10-12.) Unlike a patent, which is presumed complete, an abstract of an academic paper is not presumed to contain all of the necessary information about the study. (*Id.* at 204:16-205:1; 897:1-3.) The failure to mention a loading

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[4] Although Dr. Aradhye said that the abstract was prepared "in anticipation" of the meeting at which it was presented, (Tr. at 672:19-24,) that does not say when it became publicly available, nor does Dr. Calabresi's acknowledgement that abstracts are published in conjunction with meetings.

dose does not, therefore, indicate that the dose was not present in the trial, but only that the presence or absence of a loading dose was not mentioned in the abstract. (*Id.* at 896:18-898:10.)

75. Kappos 2006 does not enable the use of 0.5 mg daily to treat RRMS because it would require undue experimentation. (*Id.* at 210:11-212:13.) "MS is a rather unpredictable disease which makes studying it all the more difficult." (*Id.* at 211:25-212:1.) Kappos does not contain any data, like an EAE study, to indicate that a lower dosage of fingolimod would work in the treatment of RRMS. (*Id.* at 212:9-13.)

76. The prior art did not tell a person of ordinary skill that a dose of 0.5 mg was likely to work. It was known in the literature that, for a drug to be effective, it has to achieve a certain level of lymphocyte depletion, and that "the dose-response relationship is very steep[,]" meaning that, if the dose was not high enough, the drug would provide no benefit. (*Id.* at 891:10-892:6.)

III. CONCLUSIONS OF LAW

A. Infringement

1. Under the Hatch-Waxman Act, "[i]t shall be an act of infringement to submit an [ANDA] . . . for a drug . . . the use of which is claimed in a patent, . . . if the purpose of such submission is to obtain approval . . . to engage in the commercial manufacture, use, or sale of a drug . . . before the expiration of such patent." 35 U.S.C. § 271(e)(2)(A).

2. "[T]he substantive determination whether actual infringement or inducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits[,]" including those under 35 U.S.C. §§ 271(a)-(c). *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003).

3. "[A] patentee seeking relief under § 271(e)(2) must prove by a preponderance of the evidence that what is to be sold will infringe." *Id.* at 1366 (internal quotation marks and citations omitted).

4. Any physician following and prescribing fingolimod according to HEC's proposed label will directly infringe.

1. Induced Infringement

5. "Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). "To prove induced infringement, the patentee must show direct infringement, and that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement." *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1363 (Fed. Cir. 2012) (internal quotation marks omitted). In the ANDA context, in which the accused product is not yet on the market, the patentee only need show infringement will occur in the future. *Warner-Lambert Co.*, 316 F.3d at 1365-66.

6. The content of the accused infringer's proposed product label controls the induced infringement inquiry, and "[t]he pertinent question is whether

the . . . label instructs users to perform the patented method." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010). "The mere existence of direct infringement by physicians, while necessary to find liability for induced infringement, is not sufficient for inducement." *Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015).

7. "FDA regulations provide guidance on how to interpret a label." *BTG Int'l Ltd. v. Amneal Pharm. LLC*, 352 F. Supp. 3d 352, 391 (D.N.J. 2018). Pursuant to such regulations, the label must contain complete instructions on dosing and administration. *See* 21 C.F.R. 201.57.

8. "[W]here a product has substantial noninfringing uses, intent to induce infringement cannot be inferred even when the alleged inducer has actual knowledge that some users of its product may be infringing the patent." *AstraZeneca*, 633 F.3d at 1059 (Fed. Cir. 2010) (internal quotation marks and alterations omitted). "Evidence of active steps . . . taken to encourage direct infringement, such as advertising an infringing use or instructing how to engage in an infringing use, show[s] an affirmative intent that the product be used to infringe[.]" *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 936 (2005) (internal quotation marks and citation omitted).

9. HEC is liable for induced infringement. HEC's proposed label instructs the user to perform every element of the patented method, demonstrating knowing inducement. (*See* Findings of Fact ("FF") ¶¶ 40-48.) The prescribing physician would

understand the label to contain the complete dosing information, and the instructions dictate the dose of the drug in question exactly as in the Patent – 0.5 mg daily without a loading dose. (*See* FF ¶¶ 43-48.) If a user follows the instructions, there will be direct infringement. Instructing use that will infringe is an active step that demonstrates a specific intent to infringe.

2. Contributory Infringement

10. As pertinent here, contributory infringement is found where: (I) there is direct infringement; (2) the accused infringer had knowledge of the patent at issue; and (3) the product has no substantial non-infringing uses. *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1320 (Fed. Cir. 2009); 35 U.S.C. § 271(c).

11. Unlike induced infringement, the mental state required for contributory infringement is mere knowledge of infringement, not necessarily intent to cause infringement. *Lifetime Indus., Inc. v. Trim-Lok Inc.*, 869 F.3d 1372, 1381 (Fed. Cir. 2017).

12. "A noninfringing use is substantial when it is not unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental." *Gruenthal GMBH v. Alkem Labs. Ltd.*, 919 F.3d 1333, 1340 (Fed. Cir. 2019) (citations and internal quotation marks omitted). "In a pharmaceutical case, the noninfringing use must be in accordance with the use for which the product is indicated." *Id.*

13. The patentee must make a prima facie showing that a product is not "suitable for substantial non-infringing use[.]" *Golden Blount, Inc. v. Robert H. Peterson Co.*, 438 F.3d 1354, 1363 (Fed. Cir. 2006). Once the patentee makes out a prima facie case, the burden of production shifts to the accused infringer to introduce evidence to demonstrate otherwise. *Id.* at 1363-64.

14. HEC is liable for contributory infringement. HEC knew of the '405 Patent and the treatment method it sets forth. (*See* FF ¶¶ 38-40.) Because the only uses for HEC's generic fingolimod product are those identified in the clinical trial section of the proposed label, there is no substantial non-infringing use for which the product is indicated. (*See* FF ¶¶ 40-43.) If a user follows the instructions on the label, there will be direct infringement.

B. Invalidity

15. "A patent is presumed to be valid, and this presumption only can be overcome by clear and convincing evidence to the contrary." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1354 (Fed. Cir. 2010) (en banc) (internal quotation marks and citations omitted).

16. "[T]he party challenging the patent bears the burden of proving invalidity by clear and convincing evidence." *Takeda Pharm. Co. v. Zydus Pharm. USA, Inc.*, 743 F.3d 1359, 1366 (Fed. Cir. 2014).

17. The Patent, which was filed in Great Britain in June 2006 and in the United States in June 2007 (FF ¶ 68 & n.3), is subject to the pre-America

Invents Act ("AIA") standards for testing validity. *See* Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284, 293 (2011) (providing that the amendments made by the Act do not take effect until 18 months after the enactment of the Act, i.e. March 16, 2013, and apply to any application for patent, and to any patent issuing thereon, that has an effective filing date after that date); 35 U.S.C. § 100(i)(B) (defining the effective filing date as the priority date).

18. The only invalidity arguments advanced by HEC are (1) that the '405 Patent has an insufficient written description for the no-loading-dose limitation and for the claimed 0.5 mg daily dose; and (2) that the '405 Patent is anticipated by the Kappos 2006 reference.

1. <u>Written Description</u>

19. Under 35 U.S.C. § 112(a), the specification of a patent "shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention."

20. "[T]he test for sufficiency [of a written description] is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad*, 598

F.3d at 1351 (internal citation and quotation marks omitted).

21. "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.* at 1351.

22. The factors to consider "for evaluating the adequacy of the" written description include "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." *Id.* (quoting *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005)).

23. A person of ordinary skill in the art "is deemed to read the words used in the patent documents with an understanding of their meaning in the field, and to have knowledge of any special meaning and usage in the field." *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998).

24. The Patent here provides a sufficient written description of the invention such that a person of ordinary skill would know that the inventors were in possession of the invention. Read as a whole, the Patent describes a daily dosage of 0.5 mg of fingolimod, without a preceding loading dose, to treat RRMS. (*See* FF ¶¶ 49-66.) A person of ordinary skill would understand that the invention contained a treatment purpose, and that the treatment is for RRMS. (*See* FF ¶¶ 50-55.) The EAE model and the Prophetic Trial demonstrate a dosage of 0.5 mg per day, a lower dosage of fingolimod than existed in the prior art. (*See* FF ¶¶ 56-60.)

The EAE model and the Prophetic Trial also both indicate to a person of ordinary skill that the claimed invention did not include the administration of a loading dose. (*See* FF ¶¶ 61-66.)

2. Anticipation

25. Pre-AIA 35 U.S.C. § 102(b) states that "[a] person shall be entitled to a patent unless . . . the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country more than one year prior to the date of the application for patent in the United States . . . " 35 U.S.C. § 102(b) (2002).

26. Here, the Patent Cooperation Treaty application was filed on June 25, 2007, (FF ¶ 68 & n.3,) so any publications that pre-date June 25, 2006, are prior art to the claims of the '405 Patent under 35 U.S.C. § 102(b).[5]

1. HEC Has Not Met Its Burden to Prove Kappos 2006 Is Prior Art

27. "Whether an asserted anticipatory document qualifies as a 'printed publication' under § 102 is a legal conclusion based on underlying factual determinations." *Cooper Cameron Corp. v. Kvaerner Oilfield Prods., Inc.*, 291 F.3d 1317, 1321 (Fed. Cir. 2002). To qualify as a printed publication under § 102(b), the publication must be publicly

[5] As stated in footnote 3, *supra*, the parties disagree about the date for analyzing what constitutes prior art. Even if I accept the later date of June 27, 2006, it does not matter to the analysis.

accessible. *Jazz Pharm., Inc. v. Amneal Pharm., LLC*, 895 F.3d 1347, 1355 (Fed. Cir. 2018). "Public accessibility is a question of fact[.]" *Id.* at 1356.

28. To be publicly accessible, the reference must be "cataloged or indexed in a meaningful way." *In re Cronyn*, 890 F.2d 1158, 1161 (Fed. Cir. 1989).

29. Hearsay is not admissible as proof of a fact unless it falls under a hearsay exception. Fed. R. Evid. 802. The residual exception to the hearsay bar provides that a hearsay statement may be admitted, even if it does not meet any other hearsay exceptions, if it "is supported by sufficient guarantees of trustworthiness" and is more probative than other pieces of evidence. Fed. R. Evid. 807. The residual hearsay exception is to be used sparingly. *United States v. Bailey*, 581 F.2d 341, 347 (3d Cir. 1978).

30. The Lee declaration was offered for the truth of the matter asserted therein and therefore is hearsay. It does not fit within one of the recognized exceptions to the rule against hearsay, nor it is supported by "sufficient guarantees of trustworthiness" to be admissible under the residual hearsay exception. Lee was not present at trial and not available for deposition, so Novartis had no opportunity to probe the trustworthiness and facts surrounding the Lee declaration. (FF ¶ 69.) The Lee declaration does not provide any information on the procedures for cataloging, indexing, or shelving and was created 12 years after the cataloging. (FF ¶¶ 69-70.)

31. HEC failed to show by clear and convincing evidence that Kappos 2006 was publicly available in June 2006 or earlier. HEC has not presented any

evidence, let alone clear and convincing evidence, of how Kappos 2006 was cataloged, and so has not met its burden to show that the reference was publicly available in June 2006 or earlier.[6] (FF ¶¶ 68-71.) HEC similarly has not shown that Kappos 2006 was otherwise publicly available. Testimony that HEC points to (*see* n.4, *supra*) certainly does not constitute clear and convincing evidence of public accessibility.

2. Even if Kappos 2006 Was Prior Art, It Does Not Anticipate the Claims of the Patent

32. "A patent is invalid for anticipation if a single prior art reference discloses each and every limitation of the claimed invention." *Schering Corp. v. Geneva Pharm.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003).

33. "Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." *Id.*

34. "A reference may anticipate inherently if a claim limitation that is not expressly disclosed is

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[6] HEC's waiver argument is not well-founded, as pointed out by Novartis. In Novartis's pretrial statement of contested facts, Novartis says that HEC bears the burden of proof that the asserted prior art references are actually prior art to the '405 patent. (D.I. 715, PTO Ex. 2 ¶ 5.) In its pretrial submission, under the heading "Statement of Issues of Fact that Remain to be Litigated[,]" HEC listed one of those issues as whether Kappos 2006 is prior art. (*Id.* Ex. 3 ¶ 59.)

necessarily present, or inherent, in the single anticipating reference." *In re Montgomery*, 677 F.3d 1375, 1379-80 (Fed. Cir. 2012) (citations and internal quotation marks omitted). "The inherent result must inevitably result from the disclosed steps; [i]nherency . . . may not be established by probabilities or possibilities." *Id.* (citations and internal quotation marks omitted).

35. "[A] patent claim cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.'" *Verizon Servs. Corp. v. Cox Fibernet Va., Inc.*, 602 F.3d 1325, 1337 (Fed. Cir. 2010) (internal quotation marks and citations omitted). To be "enabled," a reference must enable one of skill in the art to make and use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988).

36. "Factors to be considered in determining whether a disclosure would require undue experimentation . . . include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* at 737.

37. HEC has failed to prove by clear and convincing evidence that Kappos 2006 discloses the no-loading-dose limitation. (FF ¶¶ 72, 74.) Kappos 2006 is a short abstract and does not preclude the use of a loading dose in the clinical trial it described. (FF ¶¶ 72, 74.)

38. HEC has also failed to prove that Kappos 2006 discloses the purpose limitations of the preambles. (FF ¶ 73.) Chief Judge Stark held that the claim preambles are a limiting statement of purpose, and that the Patent is "directed toward and limited to treating MS[.]" (D.I. 561 at 8 & n.3.). Kappos 2006, on the other hand, discloses a test. A person of skill would not have read Kappos 2006 as disclosing a treatment for RRMS. As Kappos 2006 describes only an early-stage clinical trial, it is too theoretical to be enabled. (FF ¶¶ 73, 75-76.)

IV. SUMMARY OF CONCLUSIONS

For the reasons set forth herein, HEC is liable for induced and contributory infringement of the '405 Patent, and the '405 Patent is not invalid for lack of written description or anticipation. Accordingly, judgment will be entered in favor of Novartis and against HEC.

/s/ Kent A. Jordan
Kent A. Jordan, Circuit Judge
Sitting by designation

August 10, 2020
Wilmington, Delaware

APPENDIX G

NOTE: This order is nonprecedential.

United States Court of Appeals for the Federal Circuit

NOVARTIS PHARMACEUTICALS CORPORATION,
Plaintiff-Appellee

v.

ACCORD HEALTHCARE, INC., AUROBINDO PHARMA LTD., AUROBINDO PHARMA USA, INC., DR. REDDY'S LABORATORIES, INC., DR. REDDY'S LABORATORIES, LTD., EMCURE PHARMACEUTICALS LTD., HERITAGE PHARMACEUTICALS INC., GLENMARK PHARMACEUTICALS INC., USA, GLENMARK PHARMACEUTICALS LIMITED, HETERO USA, INC., HETERO LABS LIMITED UNIT-V, HETERO LABS LIMITED, MYLAN PHARMACEUTICALS, INC., PRINSTON PHARMACEUTICAL INC., STRIDES GLOBAL PHARMA PRIVATE LIMITED, STRIDES PHARMA, INC., TORRENT PHARMA INC., TORRENT PHARMACEUTICALS LTD., ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., APOTEX INC., APOTEX CORP., SUN PHARMACEUTICAL INDUSTRIES, LTD., SUN PHARMACEUTICAL INDUSTRIES INC., SUN PHARMA GLOBAL FZE,
Defendants

HEC PHARM CO., LTD., HEC PHARM USA INC.,
Defendants-Appellants

2021-1070

Appeal from the United States District Court for the District of Delaware in No. 1:18-cv-01043-KAJ, Circuit Judge Kent A. Jordan.

ON PETITION FOR PANEL REHEARING AND REHEARING EN BANC

(Filed Sep. 20, 2022)

Before MOORE, *Chief Judge*, NEWMAN, LOURIE, LINN[1], DYK, PROST, REYNA, TARANTO, CHEN, HUGHES, STOLL, and CUNNINGHAM, *Circuit Judges*.[2]

PER CURIAM.

ORDER

Novartis Pharmaceuticals Corporation filed a combined petition for panel rehearing and rehearing en banc.

Law Professors and Civil Procedure Scholars David Hricik, Roger M. Baron, Lonny Hoffman, Jeffrey W. Stempel, Christa Laser, Emil J. Ali, and Dane

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[1] Circuit Judge Linn participated only in the decision on the petition for panel rehearing.

[2] Circuit Judge Stark did not participate.

Ciolino re-quested leave to file a brief as amici curiae which the court granted.

Intellectual Property Law Professors Martin J. Adelman, Emily Michiko Morris, Adam Mossoff, Kristen Osenga, Mark F. Schultz, Ted Sichelman, and Joshua Kresh also requested leave to file a brief as amici curiae which the court granted.

A response to the petition was invited by the court and filed by HEC Pharm Co., Ltd and HEC Pharm USA Inc. The petition was referred to the panel that heard the appeal, and thereafter the petition for rehearing en banc was referred to the circuit judges who are in regular active service.

Upon consideration thereof,

IT IS ORDERED THAT:

The petition for panel rehearing is denied.

The petition for rehearing en banc is denied.

The mandate of the court will issue September 27, 2022.

FOR THE COURT

September 20, 2022
Date

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court