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]

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

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[1] Novartis sued several other defendants who had also filed ANDA applications. The cases as to those other defendants all settled or were stayed prior to trial, which proceeded only as to HEC.

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, 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

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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.

0.3 mg/kg" or "administered p.o. at 0.3 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.

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

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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.

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

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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.

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.

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

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[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; s*ee 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.").

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 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,* 465 F.2d 899, 902 (C.C.P.A. 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*. at1348–49.

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 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

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

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. 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]

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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 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

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 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

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using antibiotics," a claim which allows some antibiotics lacks written description support. *Id.*

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 dosage" and the negative loading dose limitation. The same logic applies to

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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.

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 long-standing 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.