NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

NOVARTIS PHARMA AG, NOVARTIS TECHNOLOGY LLC, NOVARTIS PHARMACEUTICALS CORPORATION,
Appellants

v.

REGENERON PHARMACEUTICALS, INC.,
Appellee

2023-1334

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2021-00816.

Decided: September 23, 2024

WILLIAM M. JAY, Goodwin Procter LLP, Washington, DC, argued for appellants. Also represented by GERARD J. CEDRONE, JOSHUA WEINGER, Boston, MA. ELIZABETH HOLLAND, Allen Overy Shearman Sterling US LLP, New York, NY; WILLIAM G. JAMES, II, Washington, DC.

ANISH R. DESAI, Weil, Gotshal & Manges LLP, New York, NY, argued for appellee. Also represented by ADAM

BANKS, ELIZABETH WEISWASSER; PRIYATA PATEL, CHRISTOPHER PEPE, Washington, DC.

Before PROST, REYNA, and CHEN, *Circuit Judges*.

CHEN, *Circuit Judge*.

Novartis Pharma AG, Novartis Technology LLC, and Novartis Pharmaceuticals Corporation (collectively, Novartis) appeal from a Patent Trial and Appeal Board (Board) final written decision finding all claims of U.S. Patent No. 9,220,631 ('631 patent) unpatentable under 35 U.S.C. § 103. *See Regeneron Pharms., Inc. v. Novartis Pharma AG*, No. IPR2021-00816, 2022 WL 18460885, at *48 (P.T.A.B. Oct. 25, 2022) (*Decision*). Novartis raises a laundry list of fact-intensive arguments. For the following reasons, we *affirm*.

I.

Novartis is the assignee of the '631 patent, which relates "to a small volume syringe such as a syringe suitable for ophthalmic injections." '631 patent col. 1 ll. 5–7. The '631 patent describes a syringe that can be used to treat ocular diseases by injecting a vascular endothelial growth factor (VEGF) antagonist into a patient's eye. *Id.* at claim 1; *id.* col. 8 l. 64 – col. 9 l. 4.

As set out in the '631 patent, syringe design has many dueling considerations. For example, a syringe and its contents must be sterile to avoid infection. *Id.* col. 1 ll. 15–18. One of the claimed ways to sterilize a syringe is to use a hydrogen peroxide sterilization process. *Id.* col. 9 ll. 49–52. But some therapeutics are sensitive to that sterilization process, so the syringe may be sealed to prevent hydrogen peroxide from interacting with the drug compound. *Id.* col. 1 ll. 31–40. A tight seal, however, can increase the amount of force required to administer the drug. That force is called the break-loose force, and a high break-loose force

is undesirable. *Id.* col. 1 ll. 36–40, col. 5 ll. 27–31. One way to reduce the break-loose force is to lubricate the syringe with silicone oil. *Id.* col. 4 ll. 48–50. But silicone oil creates its own issues for eye injections because it can cause complications if it gets into a patient's eye. *Id.* col. 3 ll. 39–42, col. 4 ll. 50–55.

Given that backdrop, the present invention claims a sterile pre-filled syringe that is used for eye injections and meets certain silicone oil and break-loose force limitations. Claims 1 and 21 are illustrative for purposes of this appeal:

> 1. A pre-filled, terminally sterilized syringe for intravitreal injection, the syringe comprising a glass body forming a barrel, a stopper and a plunger and containing an ophthalmic solution which comprises a VEGF-antagonist, wherein:
>
> > (a) the syringe has a nominal maximum fill volume of between about 0.5 ml and about 1 ml,
> >
> > (b) the syringe barrel comprises from about 1 µg to 100 µg silicone oil,
> >
> > (c) the VEGF antagonist solution comprises no more than 2 particles >50 µm in diameter per ml and wherein the syringe has a stopper break loose force of less than about 11N.
>
> 21. A blister pack comprising a pre-filled syringe according to claim 17, wherein the syringe has been sterili[z]ed using EtO or H_2O_2 with a Sterility Assurance Level of at least 10^{-6}.

Id. at claims 1, 21.

Regeneron Pharmaceuticals, Inc., (Regeneron) petitioned for, and the Board instituted, *inter partes* review of all claims of the '631 patent. Regeneron asserted several

different grounds of unpatentability under 35 U.S.C. § 103. *Decision*, 2022 WL 18460885, at *2.

Before the Board, Novartis did not meaningfully dispute that all limitations are disclosed in the prior art. At a high level, Sigg[1] discloses a pre-filled terminally sterilized syringe containing a VEGF-antagonist, and Boulange[2] teaches a stopper with the claimed silicone oil and break-loose force limitations. *Id.* at *20. But Novartis argued that a skilled artisan would not have been motivated to combine the prior art with a reasonable expectation of success in achieving the claimed invention. Novartis also contended that its evidence of objective indicia of nonobviousness counseled against finding the claimed invention obvious.

In a 128-page opinion, the Board found all claims unpatentable under 35 U.S.C. § 103 over combinations of prior art references that all include Sigg and Boulange. Specifically, the Board concluded that a skilled artisan would have been motivated to combine Sigg's terminally sterilized pre-filled syringe with one of Boulange's stopper configurations, Stopper C, which has the claimed stopper with a break-loose force of less than 11N. The Board found that Boulange's baked-on siliconization method, used with its Stopper C, would help reduce the amount of silicone oil, which a skilled artisan would have wanted to minimize to avoid negative interactions with the drug product. *Id.* at *20–21. The Board also found that a skilled artisan would have had a reasonable expectation of success with this combination because Boulange's Stopper C was sealed tightly enough to be terminally sterilized using Sigg's vaporized hydrogen peroxide sterilization process. *Id.* at *23–25. After considering Novartis's objective-indicia evidence, the Board concluded that "[t]he stronger evidence of

---

1 PCT Patent Publication No. WO 2011/006877.

2 PCT Patent Publication No. WO 2009/030976.

obviousness cannot be overcome with the weaker evidence of long-felt need and failure of others." *Id.* at *37. Based on these findings, the Board did not address Regeneron's alternative grounds of unpatentability.

Novartis appeals the Board's decision, raising thirteen arguments, some of which also include additional sub-arguments. None of these arguments is persuasive, but we address only Novartis's principal arguments. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

II.

Novartis first argues that the Board erred in finding a motivation to combine Sigg and Boulange because, in Novartis's view, the prior art teaches away from combining those references. "What the prior art teaches, whether it teaches away from the claimed invention, and whether it motivates a combination of teachings from different references are questions of fact." *In re Fulton*, 391 F.3d 1195, 1199–200 (Fed. Cir. 2004). We review the Board's factual findings for substantial evidence. *PersonalWeb Techs., LLC v. Apple, Inc.*, 917 F.3d 1376, 1381 (Fed. Cir. 2019). Substantial evidence review asks "whether a reasonable fact finder could have arrived at the agency's decision, which requires examination of the record as a whole, taking into account evidence that both justifies and detracts from an agency's decision." *Id.* (citation omitted).

The Board found a motivation to combine Sigg's sterilization process with Boulange's Stopper C because Boulange's baked-on siliconization process "would help reduce the amount of 'residual' or 'free' silicone oil that can enter the protein formulation and cause negative effects." *Decision*, 2022 WL 18460885, at *21. Novartis contends three pieces of evidence allegedly teach away from using Boulange's Stopper C. We address each in turn.

First, Boulange discloses that Stopper C's break-loose force increased from 4.7N to 8.4N over the equivalent of

three months. This data is presented in Table 5. J.A. 3943. Novartis contends this data teaches away from using Stopper C because a skilled artisan would want a consistent break-loose force over a syringe's shelf life.

Substantial evidence supports the Board's finding that this evidence does not teach away from using Stopper C. At the outset, we note that claim 1 does not require a consistent force over time. Rather, as the Board recognized, the claim language merely requires a break-loose force of less than about 11N, and a break-loose force of 8.4N meets that claim limitation. The '631 patent's written description also provides that forces less than 20N were known in the prior art to be acceptable for intravitreal injections. '631 patent col. 5 ll. 35–38. That disclosure supports the Board's finding that a break-loose force of 8.4N would not teach away from using Stopper C. The Board also credited the testimony of Regeneron's expert witness, Mr. Koller, that most pre-filled syringes are expected to experience some amount of force increase over their shelf life. Novartis did not submit any evidence showing that a skilled artisan would have been dissuaded from using a syringe that has a roughly 4N increase in break-loose force over time. Oral Arg. at 4:56–5:17 (available at https://oralarguments.cafc.uscourts.gov/default.aspx?fl=23-1334_08062024.mp3). On this record, substantial evidence supports the Board's finding.

Second, following the results disclosed in Table 5, Boulange states that Stopper C was "markedly inferior" to Stopper B1. J.A. 3943. Novartis contends this statement teaches away from using Stopper C because a skilled artisan would have been motivated to use Stopper B1 instead of Stopper C.

Substantial evidence supports the Board's finding that this evidence does not teach away from using Stopper C. "In assessing whether prior art teaches away, that 'better alternatives exist in the prior art does not mean that an

inferior combination is inapt for obviousness purposes.'" *Bayer Pharma AG v. Watson Lab'ys, Inc.*, 874 F.3d 1316, 1327 (Fed. Cir. 2017) (quoting *In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012)). The Board credited Mr. Koller's expert testimony to find that a skilled artisan would have been motivated to use Stopper C because it was comprised of rubber and coated with silicone oil—a common stopper design in the prior art. *Decision*, 2022 WL 18460885, at *22. Plus, Stopper C's break-loose force was within the claimed "about 11N" and lower than the '631 patent's disclosure of 20N being a known, acceptable break-loose force for intravitreal injections. *Id.* In view of the foregoing, the Board reasonably found that a skilled artisan "would understand Stopper C is an acceptable alternative to Stopper B1 . . . even though it is categorized as 'markedly inferior' to Stopper B1." *Id.*

Finally, Boulange states that Stopper C's "friction forces . . . were relatively high, something which does not appear to be acceptable for a medical device." J.A. 3945. This statement came after the results presented in Table 7, and in the experiment that generated those results, Stopper C was not siliconized (i.e., lubricated with silicone oil). *Decision*, 2022 WL 18460885, at *22. In contrast, Stopper C was siliconized for the experiment that generated the results in Table 5, which—as already discussed—the Board found did not teach away from using Stopper C. Because a skilled artisan would be considering using siliconized Stopper C, the Board reasonably found that this statement about Table 7's results did not teach away from the results disclosed in Table 5.

III.

Novartis challenges the Board's finding of a reasonable expectation of success in combining Sigg and Boulange to achieve the claimed invention. We review the Board's finding of a reasonable expectation of success for substantial

evidence. *Intelligent Bio-Systems, Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1366 (Fed. Cir. 2016).

The Board found that a skilled artisan would have had a reasonable expectation of success because Boulange's Stopper C was sealed tightly enough to be terminally sterilized using Sigg's vaporized hydrogen peroxide sterilization process. *Decision*, 2022 WL 18460885, at *23–25. Novartis contends the Board erred because Boulange's syringes were not sufficiently gas-tight to be able to use Sigg's sterilization process.

Novartis's argument appears to be premised on an incorrect view of the claim term "terminally sterilized." Relying on Sigg, Novartis notes that very few products have the "required tightness . . . to avoid ingress of sterilizing gasses into the" pre-filled syringe. Appellant's Br. 43–44. But the Board construed "terminally sterilized" to require only *minimizing* the contact between the drug product and the sterilizing agent, and Novartis does not challenge this construction on appeal. *Decision*, 2022 WL 18460885, at *6. Thus, the Board did not need to find a reasonable expectation of success in "avoiding ingress of sterilizing gases"; it needed to find only a reasonable expectation of success in "minimizing" the ingress of sterilizing gases.

Substantial evidence supports the Board's finding of a reasonable expectation of success. The Board credited Mr. Koller's testimony that it was standard to design prefilled syringes to be gas-tight to protect the drug from degrading over its shelf life and to prevent sterilizing gas from entering the syringe. *Id.* at *24. Boulange also supports the Board's finding by describing that lower breakloose forces are achievable in the invention "without having to add lubricant and *while preserving the tightness* of the contact region between said two parts." *Id.* (quoting J.A. 3930). The Board's finding is further buttressed by the fact that the record evidence "does not demonstrate that any special tightness or specific stopper material, coating,

or dimensions[] would have been required to achieve terminal sterilization." *Id.* at *25.

IV.

Novartis next challenges the Board's finding that Sigg discloses claim 21's limitation of achieving a sterility assurance level of at least 10^{-6} using vaporized hydrogen peroxide. We review the Board's findings about the scope and content of the prior art for substantial evidence. *Ethicon Endo-Surgery, Inc. v. Covidien LP*, 812 F.3d 1023, 1028, 1034 (Fed. Cir. 2016).

The Board found that Sigg discloses this limitation because Sigg defines sterility for a health care product as achieving a sterility assurance level of 10^{-6} and describes vaporized hydrogen peroxide as a "sterilization" treatment. *Decision*, 2022 WL 18460885, at *42. Relying on expert witness testimony, the Board also determined that a skilled artisan would have known a sterility assurance level of 10^{-6} was based on regulatory requirements for health care products, and therefore pre-filled syringes are required to meet that sterility assurance level. *Id.* Substantial evidence supports these findings.

Novartis's main argument is that it disagrees with Mr. Koller's testimony that a skilled artisan knows sterilization refers to a sterility assurance level of 10^{-6} whereas sanitization refers to a sterility assurance level of 10^{-3}. Novartis points out that Sigg at one-point states that the two terms are "interchangeable," so Novartis posits that they cannot refer to different sterility assurance levels.

This argument ignores the applicable standard of review. Substantial evidence supports the Board's finding, and on the facts of this case, one inconsistent piece of evidence does not undermine that finding.

V.

We have considered Novartis's remaining arguments and find them unpersuasive.[3] For the foregoing reasons, we *affirm* the Board's decision.

AFFIRMED

[3] Two of those arguments are worth mentioning. First, Novartis argues that the Board erred in relying on non-prior art. Substantial evidence supports the Board's findings even ignoring the alleged non-prior art evidence. Second, on objective indicia of nonobviousness, the parties extensively redacted this portion of the public version of the Board's decision, but we note that substantial evidence supports the Board's findings on this matter as well.