UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FRESENIUS KABI USA, LLC and FRESENIUS KABI SWISSBIOSIM GmbH
Petitioners,

v.

COHERUS BIOSCIENCES, INC.
Patent Owner.

PGR2019-00064

Patent No. 10,155,039

Title: STABLE AQUEOUS FORMULATIONS OF ADALIMUMAB

PETITIONERS' REQUEST FOR REHEARING OF THE BOARD'S DECISION "DENYING INSTITUTION OF POST-GRANT REVIEW"

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I. PRECISE RELIEF REQUESTED

Petitioners Fresenius Kabi USA, LLC and Fresenius Kabi SwissBioSim GmbH (collectively, "Petitioners") respectfully request rehearing of this Board's Decision Denying Institution of Post-Grant Review of claims 1–12 of U.S. Patent No. 10,155,039 ("the '039 patent") under 35 U.S.C. § 112. *Fresenius Kabi USA, LLC et al. v. Coherus Biosciences, Inc.*, PGR2019-00064, Paper 10 (PTAB March 19, 2020) (the "Decision"), and institution of the challenged claims. Petitioners respectfully submit that a rehearing is appropriate because the Decision erroneously excluded the inventors' preferred embodiments from the claims, misapplied the law regarding the written description and enablement requirements of 35 U.S.C. § 112, and is not supported by substantial evidence in the record.

II. THE BOARD'S FINDING THAT THE SPECIFICATION ADEQUATELY DESCRIBED AND ENABLED THE "STABLE" FORMULATIONS OF CLAIMS 1–12 IS BASED ON AN ERROR OF LAW AND IS NOT SUPPORTED BY SUBSTANTIAL EVIDENCE

Under 37 C.F.R. § 42.71(c), "[w]hen rehearing a decision on petition, a panel will review the decision for an abuse of discretion." "An abuse of discretion occurs where the decision is based on an erroneous interpretation of the law, on factual findings that are not supported by substantial evidence, or represents an unreasonable judgment in weighing relevant factors." *Gose v. U.S. Postal Serv.*, 451 F.3d 831, 836 (Fed. Cir. 2006) (internal quotations omitted).

Here, after rejecting Petitioner's proposed construction of "stable" in claims

1–12, the Board clearly erred when it held that embodiments having the inventors' preferred levels of stability were excluded from the claims. Because of that error, the Board wrongly concluded that the specification adequately described and enabled the full scope of "stable" formulations covered by claims 1–12.

A. The Board Erred by Holding That, Under Its Claim Construction, The Claims Exclude The Identified Preferred Embodiments

The Decision rests almost entirely on a single error of law. According to the Board, because the term "stable" does not *limit* the claims to the preferred embodiments, the claims do not *include* the preferred embodiments. Respectfully, the Board's view that the claims do not include the inventors' preferred embodiments does not follow from its own claim construction, the portions of the specification on which it relies, or long-established law disfavoring claim constructions that exclude preferred embodiments.

The Board held that "the term 'stable' is defined to only require a minimum level of stability (i.e., a loss of no more than 20% of activity)." Denial of Institution Opinion ("D.I. Op.") at 9. The Board explained that it was "unpersuaded by Petitioner's argument that the term 'stable' should be construed to include [the inventors' most-preferred] formulations that do not lose more than 5% of their activity during two years of long-term storage" because the specification makes clear that less stable formulations fall within the scope of the claims. *Id.* at 8–9. For example, "portions of the specification indicate that the

required stability may be determined by a comparison to the commercial formulation of adalimumab known in the prior art, i.e., Humira," *id.* at 8, including those that note that "long term storage" should be understood to "*further include* stable storage durations that are at least comparable to" the shelf life of "currently available commercial formulations of adalimumab." *Id.* at 9 (emphasis added). The Board found no "intrinsic or extrinsic evidence of record suggesting that the applicant intended to require that the claimed formulations *must* be able to achieve the [most-preferred] highest amount of stability over the longest time period identified in the specification." *Id.* at 10 (emphasis added).

Petitioners acknowledge (as they did in the Petition, *see* Pet. 11–12) that the claimed "stable" formulations "further include" those that are as stable as Humira, as well as those that lose no more than 20% of activity during storage—the minimum that the inventors described as being within the scope of their invention. These facts, however, do not compel—or even support—the conclusion that "stable" *excludes* the inventors' *preferred* embodiments, including their most-preferred embodiments that do not lose more than 5% of their activity during two years of long-term storage. The Board did not construe "stable" to be *limited* to formulations that are as stable as Humira or lose 20% of activity upon storage. And even if 20% loss after storage is a lower bound for the claims, the specification nowhere indicates—and the Board did not hold—that this is an *upper*

bound. Indeed, the fact that 20% loss after storage does not exclude more-stable formulations is implicit from the Board's inclusion of formulations that are as stable as Humira. Nowhere do the inventors state or does the Board conclude that Humira loses 20% of activity after storage.

The Board's erroneous view of its construction of "stable" as excluding the inventors' preferred embodiments also contravenes well-established law. Claims should almost never be construed so as to exclude preferred embodiments described in the specification. *See, e.g.*, *SynQor, Inc. v. Artesyn Tech., Inc.*, 709 F.3d 1365, 1378–79 (Fed. Cir. 2013) ("A claim construction that excludes the preferred embodiment is rarely, if ever, correct and would require highly persuasive evidentiary support.") (quotation omitted). There is no support for such a construction here, where far from unambiguously disclaiming their preferred embodiments, the inventors *explicitly defined "stable" to include them*. As explained in the Petition, the inventors acted as their own lexicographers to make clear that "stable" encompasses a range of preferred embodiments, including most-preferred embodiments that lose no more than 5% of activity over two years of long-term storage:

> The term 'stable' with respect to long-term storage is understood to mean that adalimumab contained in the pharmaceutical compositions does not lose more than 20%, or more preferably 15%, or even more preferably 10%, and most preferably 5% of its activity relative to

activity of the composition at the beginning of storage.

See '039 patent, 9:28–34; Pet. 10; Ex. 1002 ¶¶ 44–51. Further, "'long term storage' . . . is understood to mean that the pharmaceutical composition can be stored for … most preferably a minimum stable shelf life of at least two years." *Id.* at 9:12–16; Pet. 11–12; Ex. 1002 ¶¶ 44–51. The Board acknowledged that these definitions control when it construed "stable" as having a lower bound of 20% loss and as including long-term storage stability comparable to Humira. While these paragraphs include the embodiments the Board cited, the inventors made clear that "stable" also includes their more- and most-preferred levels of stability.

Given the inventors' express definitions, the Board also clearly erred when it "agree[d] with Patent Owner that '[a] POSA would not interpret the claims as covering a genus of formulations having a range of different stabilities . . . , especially because the claims simply do not recite a range of stability values to be achieved over different periods of time." D.I. Op. 9 (quoting Prelim. Resp. 15). A claim need not recite a range to be a genus claim. If a claim encompasses more than one disclosed embodiment, it is a genus claim. *See* MPEP § 806.04(e) ("[A]*claim may encompass two or more of the disclosed embodiments (and thus be designated a generic or genus claim*"). Here, since the claims include all of the preferred embodiments, and those embodiments span a range of stabilities, the claims span a range of stabilities. Pet. 12; Ex. 1002 ¶¶ 51, 135. Tellingly, under

the Board's construction, the broadest claim—claim 1—would be anticipated by a narrow species in the prior-art: a formulation that met all of the ingredient limitations of the claim and achieved the inventors' most-preferred level of stability (5% loss over two years of storage). It and the other claims are clearly genus claims, and it was an abuse of discretion to hold otherwise.

B. The Board Erred In Finding That The Specification Sufficiently Enables Claims 1–12

The Board erred when it held that "we do not find that the claims must necessarily be enabled" for formulations that meet the most-preferred level of stability, reasoning that "the specification only discloses that a loss of no more than 5% is 'most preferabl[e],' but is not otherwise required to achieve a stable pharmaceutical composition." D.I. Op. 17. The inventors were required to enable *the full scope of their claims. See Trustees of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1363 (Fed. Cir. 2018) ("Our precedents make clear that the specification must enable the full scope of the claimed invention."). Having defined the term "stable" in the specification so that the claims encompass the most-preferred level of stability, the inventors were required to enable, *e.g.*, this preferred embodiment. *Id.* at 1365 ("Having obtained a claim construction that included a purely amorphous layer within the scope of the claim, BU then needed to successfully defend against an enablement challenge as to the claim's full scope"). To hold otherwise would allow the Patent Owner to exclude the public

from practicing preferred embodiments described in the specification without giving the required *quid pro quo* of actually disclosing how to make them.

Crucially, Patent Owner did not contend, and the Board did not hold, that the specification discloses how to make the most-preferred formulations that lose no more than 5% of activity over two years of storage. *See* D.I. Op. 16–17. While, as the Board noted, there is accelerated testing of one embodiment of claim 1—formulation D-12—which purportedly shows it to be as stable as Humira, the specification does not disclose any information from which a POSA could conclude that Humira loses no more than 5% of activity over two years of storage, or that formulation D-12 meets this level of stability. As explained in the Petition and in the declaration of Dr. Schoneich, and as the Patent Owner repeatedly emphasized during prosecution, the level of stability that a particular combination of ingredients will achieve is unpredictable. Pet. 41–42; Ex. 1002 ¶¶ 150–51, 186. According to Dr. Schoneich, a POSA would not have been able to conclude that formulation D-12 loses no more than 5% of activity after two years of storage, and would not have known from the specification which of the many millions of possible combinations of buffer, sugar, adalimumab and pH levels would achieve this stability. Ex. 1002 ¶¶ 148–53, 157–68, 185–87. While the Board is correct that some experimentation is permitted, here a POSA seeking to practice the most-preferred embodiments is essentially left to perform the same laborious trial-and-

error experimentation that the inventors engaged in and received a patent for. Pet. 60–61; Ex. 1002 ¶¶ 186–87. This is the antithesis of enablement. *See MorphoSys AG v. Janssen Biotech, Inc.*, 358 F. Supp. 3d 354, 371–72 (D. Del. 2019) (finding lack of enablement where a POSA "would have to do essentially the same amount of work as the inventors").

The Board should have found that Petitioners were reasonably likely to prevail on their enablement challenge to claims 1–12 and instituted the Petition.

C. The Board Erred In Finding That The Specification Provides a Sufficient Written Description For Claims 1–12

Relatedly, the Board's erroneous exclusion of the inventors' more- and most-preferred embodiments from the claims led it to reach the wrong result on Petitioners' written-description challenge to claims 1–12.

While the Board is correct that a patent need not "include test results or working examples demonstrating stability for *every possible composition* covered by the claims," D.I Op. 13 (emphasis added), the specification must clearly demonstrate possession of the *full scope* of the claims. *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1301 (Fed. Cir. 2014) (written description must "support the full scope of the claims."). Here, since the claims require that the formulations be "stable," and the inventors expressly defined that term to include embodiments having their most-preferred stability, the specification must clearly demonstrate to a POSA that the inventors actually

possessed a formulation with their most-preferred stability. *See Nuvo Pharm. (Ireland) Designated Activity Co. v. Dr. Reddy's Labs. Inc.*, 923 F.3d 1380, 1381 (Fed. Cir. 2019) (holding that where a patentee claims a specific result, the specification must demonstrate to POSAs that the inventors were in possession of an invention that actually achieves that result). The inventors could have chosen to limit their claims to, e.g., formulations as stable as Humira, but did not. To allow the inventors claim scope that covers their preferred embodiments but not require them to meet the requirements of § 112 would invite inventors to claim speculative embodiments with favorable properties that they themselves have not yet achieved. This cannot be squared with the policies behind § 112. *See Nuvo*, 923 F.3d at 1376–77 (written description requirement is part of bargain with the public, "so that the public will know . . . [the inventor] has truly made the claimed invention").

Here, the Board concluded that the testing of a single formulation, D-12, was sufficient to demonstrate possession of all of the formulations of claim 1 because that testing purportedly demonstrated that D-12 was as stable as the Humira control formulation. D.I. Op. 12–14. But the claims are far broader in scope and include formulations that are more stable than Humira. Indeed, the very problem that the inventors allegedly solved was that prior-art formulations of adalimumab (which include Humira) lose activity during long-term storage. Pet. 4; Ex. 1002 ¶¶ 39, 44. As explained in the Petition and in Dr. Schoneich's declaration, a POSA

would not have been able to conclude from the specification that any of the disclosed formulations, including those as stable as Humira, meet the inventors' most-preferred levels of stability. Pet. 31–44; Ex. 1002 ¶¶ 154–63. Patent Owner did not rebut this extrinsic evidence and the Board did not conclude otherwise. Thus, the Board should have found that Petitioners are reasonably likely to prevail on their written description challenge and instituted the Petition.

III. THE BOARD'S FINDING THAT THE SPECIFICATION ADEQUATELY DESCRIBED AND ENABLED THE ACETATE FORMULATIONS OF CLAIMS 9–12 IS NOT SUPPORTED BY SUBSTANTIAL EVIDENCE

The Board's conclusion that the specification adequately described and enabled the formulations of claims 9–12, which are limited to those that include acetate buffer and sucrose, was also not supported by substantial evidence. The Board essentially ignored Petitioners' specific arguments concerning the lack of § 112 support for claims 9–12. *See* Pet. 55, 58–61. Regardless of the Board's construction of the term "stable," claims 9–12 require the formulation to achieve that stability using acetate as the buffer. The Board failed to weigh two key facts: (1) the specification does not disclose *any* embodiment of the claimed acetate formulations, and (2) the specification *expressly teaches away* from the use of acetate as a stabilizing buffer. Pet. 21–27, 50, 55; Ex. 1002 ¶ 178.

A. The Board Improperly Ignored The Intrinsic Evidence Concerning The Specific Formulations Of Claims 9–12

Neither the Board's decision nor Patent Owner's Preliminary Response point

to any disclosure of a formulation that contains all of the elements of claims 9–12. Instead, the Board's finding that there was adequate description of compositions with an acetate buffer relies on two parts of the specification: (1) that formulations containing acetate were disclosed in Table E (Prelim. Resp. 61), and (2) a bald statement unsupported by test data that "acetate is also a suitable replacement for the citrate phosphate buffer combination" in Table A. Prelim. Resp. 60 (citing 21:40–47). These disclosures *do not describe formulations that meet the limitations of claims 9–12*. Pet. 16–18, 55; Ex. 1002 ¶¶ 154–55, 178. They therefore cannot constitute substantial evidence to support the Board's findings.

As explained in the Petition and Dr. Schoneich's declaration, none of the formulations in Table E contain all elements of claims 9–12. Pet. 55; Ex. 1002 ¶ 178. The Board relied on Patent Owner's identification of formulations 3, 9, and 11, but ignored the crucial differences between these compositions and the compositions of claims 9–12. These differences concern the very ingredients that are allegedly critical to stability and are alleged to be the hallmarks of the inventors' contribution to the field. Formulation 3, for example, contains mannitol and NaCl, which the inventors expressly excluded from their entire invention. Ex. 1002 ¶ 178. Formulations 9 and 11 do not contain polysorbate 80, another key ingredient. *Id.* None of the three formulations include sucrose, which is the sugar required by claims 9–12 that allegedly distinguishes the claimed formulations from

prior-art formulations that use mannitol. Ex. 1001 at col. 38; Ex. 1002 ¶¶ 178–79; Pet. 18. In short, none of the "working examples" that the Board concluded demonstrate the claimed stability are of the alleged invention of claims 9–12.

A POSA looking to determine how to combine acetate and sucrose into the stable formulation of claims 9–12 would have found no guidance. Ex. 1002 ¶¶ 144, 151, 184; Pet. 38. This lack of disclosure is especially problematic for a POSA, since combining even known formulation ingredients in new ways may have unpredictable effects on stability. Ex. 1002 ¶¶ 145, 148–53; Pet. 38. Patent Owner relied on this unpredictability to obtain the patent claims. Pet. 7, 41; Ex. 1002 ¶¶ 143, 150. The Board does not mention, and completely failed to consider, Dr. Schoneich's unrebutted declaration and this unpredictability in its analysis.

Moreover, apart from the lack of guidance, the specification *expressly teaches away from the use of acetate*. The sole conclusion about acetate drawn by the inventors from their experiments was that "acetate is a strong destabilizer . . . " Ex. 1001 at 65:43–44; Ex. 1002 ¶¶ 144, 178–79; Pet. 50, 55, 59. Beyond this express teaching, the specification teaches away from the use of acetate by excluding from the claims other ingredients identified as "destabilizing," like NaCl and citrate and phosphate buffers, Pet. 62–63; Ex. 1001 at claims 1–12, and by omitting acetate from its list of preferred ingredients. Pet. 55.

In light of Patent Owner's arguments during prosecution that antibody stability is unpredictable (*see* Pet. 41–42), there is a disconnect between the statements on which the Board relies—that acetate buffer "may" be used in the claimed formulations—and the data and PLS analyses which, according to the inventors, show that acetate strongly destabilizes such formulations. The Board's analysis does not address this fundamental contradiction.

B. The Board's Conclusion That Claims 9–12 Have Written Description Support is Flawed

The Board's conclusion regarding the written description support for claims 9–12 misapplies the governing law. General disclosures of elements of a claim, without guidance on how to combine the elements as claimed, do not show that the inventors had possession of the alleged invention. Pet. 24 (citing *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996) ("laundry list" of claim elements does not suffice where there are no "blaze marks" directing them to be combined as claimed)). A specification that requires "picking and choosing to arrive at the claimed invention" does not support a conclusion that the invention was described. *FWP IP ApS v. Biogen MA, Inc.*, 749 F. App'x 969, 973 (Fed. Cir. 2018).

Here, the specification does not include any formulation that contains acetate and also meets the other limitations of claims 9–12. A POSA would have to "pick and choose" from among a large number of possible ingredients to arrive at the claimed combinations, without any guidance as to which would be "stable" in the

presence of a "strong destabilizer" like acetate. Pet. 24; Ex. 1002 ¶¶ 151, 178–79. Petitioners explained that a POSA would not have understood the inventors to be in possession of acetate buffer formulations. Pet. 55; Ex. 1002 ¶¶ 178–80. The Board's decision, however, does not rely on any teaching in the specification showing that the inventors had possession of the compositions of claims 9–12.

The Board's analyses of the representative species test and the common structural features test are not relevant to claims 9–12. While the Board found at least one example of a "stable" formulation that met the limitations of claim 1, there are *no* examples that are representative of claims 9–12. Pet. 18, 38–39, 45–46, 55. Similarly, the Board does not point to any disclosures that identify features of the combinations claimed in claims 9–12 that correlate with stability. Acetate is in fact identified as a "strong destabilizer." Pet. 38–39, 45–46, 55. The Board's decision fails to apply either test for claims 9–12. Therefore, the Board misapplied the law in reaching its conclusion that these claims had adequate written description because it did not apply either test for claims 9–12.

C. The Board's Conclusion That Claims 9–12 Are Enabled is Also Erroneous

The Board also clearly erred when it ignored the inventors' teaching away from the use of acetate in its analysis of whether claims 9–12 are enabled.

The specification contains no teaching of how a POSA should correct for the destabilizing effects of acetate identified in the specification, and no guidance as to

which other ingredients to use or avoid with this particular destabilizing buffer. Pet. 55; Ex. 1002 ¶¶ 144, 151, 184; s*ee also Enzo Life Sciences, Inc. v. Roche Molecular Sys., Inc.*, 928 F.3d 1340, 1346–49 (Fed. Cir. 2019) (finding lack of enabling disclosure where "guidance as to how such variables would or would not impact the functionality of the claimed [invention] is sparse."). As Dr. Schoneich explained, in light of the conclusion that acetate was destabilizing, a POSA would have doubted whether acetate would work in a stable formulation, and would have had to engage in undue experimentation to try to devise a solution to the destabilization documented in the specification. Ex. 1002 ¶¶ 148, 151, 181.

Statements in a specification that teach away from the claimed subject matter are clear evidence that undue experimentation would be required to practice the claim. *Liebel-Flarsheim Co. v. Medrad, Inc.*, 481 F.3d 1371, 1379 (Fed. Cir. 2007); *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1244 (Fed. Cir. 2003). Thus, far from ignoring the statements teaching away from acetate, the Board should have found them to be compelling evidence that undue experimentation would be required to make formulations of claims 9–12. The Board's conclusion that claims 9–12 are enabled is thus unsupported by substantial evidence.

Respectfully submitted,

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), the undersigned hereby certifies that on this 17th day of April, 2020, a copy of this PETITIONERS' REQUEST FOR REHEARING OF THE BOARD'S DECISION "DENYING INSTITUTION OF POST-GRANT REVIEW" was served by email on the lead and back up counsel for Patent Owner at:

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