

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

APOTEX INC. and APOTEX CORP.,
Petitioner,

v.

AMGEN INC. and AMGEN MANUFACTURING LIMITED,
Patent Owner.

Case IPR2016-01542
Patent 8,952,138 B2

Before JAMES T. MOORE, CHRISTOPHER G. PAULRAJ, and
KRISTI L. R. SAWERT, *Administrative Patent Judges*.

MOORE, *Administrative Patent Judge*.

DECISION
Denying Petitioner's Request for Rehearing
37 C.F.R. § 42.71(d)
and
Amending Prior Decision
37 C.F.R. § 42.5(a)

I. INTRODUCTION

A Final Written Decision in this matter was rendered February 15, 2018, in which we found claims 1–17 and 19–24 of the subject patent unpatentable. Paper 60. Petitioner, Apotex, Inc. and Apotex Corp.¹ timely filed a Request for Rehearing under 37 C.F.R. § 42.71(d) on March 16, 2018. Paper 61 (“Reh’g Req.”). Familiarity with these papers is presumed.

The grounds for rehearing (1) relate to the Board’s interpretation of the term “non-aerobic conditions” and (2) the Board’s conclusion that Petitioner had not shown that claim 18 was unpatentable. *Id.*, 1.

We ordered additional briefing, including an opposition to the rehearing request, and briefs from both Patent Owner and Petitioner explaining the meaning of the term “non-aerobic conditions.” Paper 63; *see also* Paper 64 (Petitioner’s brief), Paper 65 (Opposition), Paper 66 (Patent Owner’s brief). For the reasons that follow, including the repeated use in the party’s pleadings of the term “non-aerobic” in a manner inconsistent with the specification, we deny the request.

We also *sua sponte* modify our Final Written Decision as below.

¹ Apotex Pharmaceuticals Holdings, Inc., Apotex Holdings, Inc., and ApoPharma USA, Inc., and Intas Pharmaceuticals Limited are said to be additional real parties in interest. Pet. 2. Hereinafter “Petitioner,” collectively.

II. STANDARD

37 C.F.R. § 42.71(d) provides that the request for rehearing must “specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, or a reply.”

III. THE REQUEST

A. Misapprehended or Overlooked

Petitioner asserts that the Board adopted an erroneous construction of “non-aerobic conditions.” Paper 61, 3. Specifically, Petitioner points out that the specification provides a special definition for “non aerobic condition” as follows:

As used herein, the term “non-aerobic condition” means any reaction or incubation condition that is performed without the intentional aeration of the mixture by mechanical or chemical means. Under non-aerobic conditions oxygen can be present, as long as it is naturally present and was not introduced into the system with the intention of adding oxygen to the system. Non-aerobic conditions can be achieved by, for example, limiting oxygen transfer to a reaction solution by limiting headspace pressure, the absence of, or limited exposure to, air or oxygen contained in the holding vessel, air or oxygen overlay, the lack of special accommodations to account for mass transfer during process scaling, or the absence of gas sparging or mixing to encourage the presence of oxygen in the reaction system. Non-aerobic conditions can also be achieved by intentionally limiting or removing oxygen from the system via chemical treatment, headspace overlays or pressurization with inert gases or vacuums, or by sparging with gases such as

argon or nitrogen, results in the reduction of oxygen concentration in the reaction mixture.

Ex. 1001, 7:20–37.

This definition is relevant to our Final Written Decision because claim 18 depends from claim 1, and recites that “the incubation is performed under non-aerobic conditions.” Ex. 1001, 18:46–47. Claim 18 is the only challenged claim we did not find to be unpatentable in this proceeding. Paper 60, 47–48. We were unaware of the special definition of the term within the specification.

Consequently, we agree with Petitioner that we overlooked this special definition contained within the record. We turn next to the second prong of the rehearing requirement.

B. Previously Addressed in a Motion, Opposition, or Reply

37 C.F.R. § 42.104 requires Petitioner to identify in the Petition “[h]ow the challenged claim is to be construed.” And although Petitioner proposed constructions for several other claim terms in the Petition, it did not include “non-aerobic conditions” among those terms. Pet. 19–28. Nonetheless, Petitioner now asserts that the “construction of terms not explicitly construed by Petitioner, including ‘non aerobic conditions’ was previously addressed in the Petition at Page 20.” Reh’g Req. 2.

We reproduce that portion of the Petition below:

In accordance with 37 C.F.R. § 42.100(b), the challenged claims must be given their broadest reasonable interpretations in light of the specification of the ’138 Patent. To be clear, any

claim terms not included in the following discussion should be given their broadest reasonable construction in light of the specification.

Pet. 20.

In our view, this general statement does not sufficiently direct our attention to the special definition of the term “non aerobic” contained in the specification of the ’138 patent. That special definition is contained along with myriad other definitions in a section spanning several columns and including multiple definitions.

The Petition, in fact, led us in a different direction, by treating the term “non-aerobic conditions” in claim 18 as have its plain and ordinary meaning, rather than the special definition provided in the specification. On page 55, where the issue of claim 18 is squarely addressed, the Petition states:

It was well known at the time of the invention that aerobic conditions could impact the redox chemistry of the refolding reaction. EX1001 at 8:3-17; EX1002 at ¶ 148. For example, *Hevehan* discloses that “[s]olutions of reduced DTT were prepared immediately prior to each experiment to minimize air oxidation.” EX1004 at 2; *see also* EX1028; EX1020.

Paper 2, 55.

This argument does not hint at the special definition. “Aerobic” and “non-aerobic” are well-known terms of art. Aerobic means “[r]equiring air or oxygen.” *See, e.g.*, Hawley’s Condensed Chemical Dictionary, 14th Edition, p. 25. Ex. 3001. More generally, aerobic is in practice understood

to mean “living, acting, or occurring only in the presence of oxygen.” *See, e.g., Webster’s New Collegiate Dictionary*, p. 19. Ex. 3002. “Non,” on the other hand means “not : reverse of : absence of.” *Id.* “Non-aerobic,” in the absence of a special definition, is the absence of oxygen.

Petitioner’s argument directing us to the effects of air oxidation as being a known negative reinforce Petitioner’s use of the plain meaning of the term “non-aerobic conditions” in the Petition.

Petitioner next points us to Exhibit 1002 ¶¶ 147–148 as addressing the issue. Exhibit 1002 is the Declaration of Dr. Robinson. Dr. Robinson states in the cited portions that:

6. Claims 18-24 Are Obvious over *Schlegl* and *Hevehan*

147. Claims 18-24 are directed to various conditions or methods relating to the incubation or isolation step of claim 1. Each of these various conditions or methods was standard methods well known in the art.

a. Claim 18: “wherein the incubation is performed under non-aerobic conditions”

148. In my opinion, it was well known at the time of the invention that aerobic conditions could impact the redox chemistry of the refolding reaction. For example, *Hevehan* teaches that “[s]olutions of reduced DTT were prepared immediately prior to each experiment to minimize air oxidation.” EX1004 at 2; see also EX1028; EX1020.

Here, the emphasis on air oxidation leads us to conclude that Dr. Robinson herself considered the term “non-aerobic” to have its commonly

known meaning of “in the absence of oxygen.” In other words, there is no direction to the Board in her testimony that a special definition existed.

Petitioner also points to Exhibit 1056 ¶ 67 in support of the proposition that it addressed the issue to the Board. Dr. Robinson states in the cited portion that:

c. Claim 18

67. One of ordinary skill knew at the time of the invention that aerobic conditions could impact the redox chemistry of the refolding reaction. Pet. 55; EX 1002, ¶ 148. Hevehan describes solutions of reduced DTT that were prepared immediately prior to each experiment to minimize air oxidation. EX1004, 2; Ex. 1028 (fermentation); Ex. 1020; see also EX1004 at 3 (also discussing fermentation). In addition, some of the earliest commercial refolding approaches involved air oxidation; it was well known from the late ‘90s that this approach could be used with metal ions. However, it was also understood that refolding yields could be low and unpredictable, making the presence of oxygen undesirable. EX1021 at 2; EX1014 at 7.

Ex. 1056 ¶ 67.

This cited paragraph also utilizes the concept that the “presence of oxygen was undesirable” as the basis for its position that claim 18’s “non-aerobic” limitation was obvious. Again, this argument and testimony does not address the issue of a special definition for “non-aerobic” to the attention of the Board.

We next turn to the Reply. Petitioner cites us to Paper 26 at 17 in support of its position that it addressed the issue to the Board:

c. Claim 18

One of ordinary skill knew at the time of the invention that aerobic conditions could impact the redox chemistry of the refolding reaction. Pet., 55; EX1002, ¶148; EX1056, ¶67. Hevehan describes solutions of reduced DTT that were prepared immediately prior to each experiment to minimize air oxidation. Pet., 55, EX1004, 2, 3; EX1028 (fermentation); EX1020. Thus, a person of ordinary skill would have been motivated to *eliminate oxygen* from the refolding reaction. EX1056, ¶67; EX1021, 2; EX1014, 7.

Paper 26, 17 (emphasis added).

To us, this is the clearest statement yet that Petitioner intended “non-aerobic” to mean the elimination of, or absence of, oxygen. Here, Petitioner specifically argues that it would have been obvious to “eliminate oxygen from the refolding reaction.”

Turning to the Institution Decision, Paper 10, the Board expressly did not construe the term “non-aerobic.” Paper 10, 10. No party raised the issue of the need to do so during the pendency of the proceeding.

On the other side, Patent Owner also did not provide any definition for “non aerobic” in its Preliminary Response, although numerous other claim terms were discussed. Paper 9, 8–18. Patent Owner’s Response (Paper 14) takes issue with Petitioner’s position concerning claim 18 in an argument that:

As for Claim 18, that claim depends from Claim 1 (which references “incubating the refold mixture”) and further requires that such “incubation is performed under non-aerobic conditions.” But there is no evidence that the combination of

Schlegl and *Hevehan* teaches this limitation. Petitioners do not rely on *Schlegl* for this limitation—nor can they, since *Schlegl* only discloses refolding tanks for incubation under aerobic conditions. As for *Hevehan*, Petitioners can only cite to a passage that—as Dr. Robinson readily admitted at deposition—bears no relationship whatsoever to the incubation of the refold mixture, as required by Claim 18. What Petitioners notably do not cite: a different *Hevehan* passage, teaching that its refolds were done aerobically.

Paper 14, 5.

Nothing in this passage points us to the special definition of “non-aerobic” within the ’138 patent specification.

Patent Owner also leads the Board toward the plain meaning of the term in its Response. Specifically:

Claim 18 recites “[t]he method of claim 1, wherein the incubation is performed under non-aerobic conditions,” *i.e.*, *conditions without oxygen*. EX2020 at ¶101. Claim 1 recites “incubating the refold mixture”; it follows that Claim 18’s incubation under non-aerobic conditions is performed after the refold mixture is made. In addition to the reasons stated above with respect to Claim 1, there are more reasons why *Schlegl* and *Hevehan*, alone or in combination, do not render obvious dependent Claim 18.

Paper 14, 46–47 (emphasis added).

Exhibit 2020 is the testimony of Dr. Willson, Patent Owner’s witness. He testifies that:

E. Schlegl and Hevehan, Alone or in Combination, Do Not Render Obvious Claim 18 of the ’138 Patent

101. Claim 18 of the '138 Patent further limits the incubation step of Claim 1 to be “performed under non-aerobic conditions,” *i.e.*, **conditions that lack oxygen**. EX1001, '138 Patent at Claim 18. Claim 1’s incubation step is with respect to the “refold mixture.” *Id.* at Claim 1. Accordingly, Claim 18 requires incubating the refold mixture under non-aerobic conditions.

Ex. 2020 ¶ 101 (bolded emphasis added).

Patent Owner, consequently, reinforces to the Board that “non-aerobic” as used in the pleadings means “without oxygen.”

We observe that Petitioner discusses that it filed an Opposition to Patent Owner’s Motion to Exclude. Reh’g Req. 2. That paper, although not specifically identified in the request for rehearing, is Paper 46. Paper 46 was filed long after the principal briefing in this proceeding was completed, and specifically concerned Paper 44 – a motion to exclude Dr. Hart’s testimony. In the opposition, for the first time, Petitioner discusses the special definition of the term “non-aerobic” contained within the specification. Paper 46, 9. However, as we did not rely upon those exhibits, we dismissed the underlying motion to exclude, and had no need to consider the opposition thereto. We therefore did not reach the opposition.

IV. Patent Owner’s Opposition

Patent Owner observes that Petitioner’s Request for Rehearing rests on arguments that were not raised in its Petition, Reply, any declaration, or other evidence. Paper 65, 2. We agree for the reasons discussed above.

Consequently, as Petitioner has not demonstrated where the issue was addressed to the Board, we deny the request for rehearing.

V. The Additional Briefing

We ordered additional briefing on the issue of claim interpretation of the term “non-aerobic conditions.” Paper 63. We did this because the term is expressly defined and we wish to ensure the decision is legally accurate and each party has had adequate opportunity to provide input on the broadest reasonable interpretation of the term.

Petitioner states that the meaning of “non-aerobic conditions” is the express definition set forth in the specification. Paper 64. Patent Owner agrees. Paper 66.

With this definition in mind, we revisit our earlier decision only as it pertains to claim 18. “[T]he courts have uniformly concluded that administrative agencies possess inherent authority to reconsider their decisions, subject to certain limitations, regardless of whether they possess explicit statutory authority to do so.” *Tokyo Kikai Seisakusho, Ltd. v. United States*, 529 F.3d 1352, 1360–61 (Fed. Cir. 2008); *see Last Best Beef, LLC v. Dudas*, 506 F.3d 333, 340–41 (4th Cir. 2007) (as a federal agency, the USPTO possesses “inherent discretion to correct its own errors and to manage its own docket”); *Ivy Sports Med., LLC v. Burwell*, 767 F.3d 81, 86 (D.C. Cir. 2014); *Macktal v. Chao*, 286 F.3d 822, 825–26 (5th Cir. 2002) (collecting cases).

Claim 18

Claim 18 depends from claim 1, and recites that “the incubation is performed under non-aerobic conditions.” Ex. 1001, 18:46–47.

Petitioner asserts that one of ordinary skill knew at the time of the invention that aerobic conditions could impact the redox chemistry of the refolding reaction, as attested by Dr. Robinson. Pet. 55, citing Ex. 1002 ¶ 148. Petitioner also observes that Hevehan describes solutions of reduced DTT that were prepared immediately prior to each experiment to minimize air oxidation. Pet. 55 (citing Ex. 1004 at 2; Ex. 1028 (fermentation); Ex. 1020, 3 (also fermentation)).

Patent Owner urges that Petitioner incorrectly asserts that the combination of Schlegl and Hevehan teaches that “incubation is performed under non-aerobic conditions.” Resp. 47. Patent Owner points out that Dr. Robinson testified during her deposition that Schlegl is “silent on the presence or absence of oxygen.” *Id.* (citing Ex. 2019 at 54:20–55:2). Moreover, it is urged that Schlegl’s figures make abundantly clear that the refolding tanks are open to air, i.e., under aerobic conditions. *Id.* (citing Ex. 1003 at Figures 1–3).

As for Hevehan, Patent Owner urges that the minimization of oxidation of DTT, a reductant, does not indicate that the refolding of the protein occurred under anaerobic conditions. Reply 47–48 (citing Ex. 2019 at 82:17–20).

Based on the undisputed construction of “non-aerobic conditions,” however, claim 18 only requires any reaction or incubation condition to be performed without the *intentional* aeration of the mixture by mechanical or chemical means. Ex. 1001, 7:20–23. Hevehan and Schlegl do not describe intentional aeration (even though oxygen may be naturally present) and thus satisfy the requirement for incubation performed under “non-aerobic” conditions.

Thus, we are persuaded that Petitioner has demonstrated that challenged claim 18 is unpatentable as obvious over Schlegl and Hevehan.

VI. CONCLUSION

We therefore alter our prior decision, and conclude that Petitioner has carried its burden of showing claim 18 is unpatentable as obvious over Schlegl and Hevehan.

VII. ORDER

Accordingly, it is:

ORDERED that

Petitioner's Request for Rehearing is DENIED.

Our prior decision is *sua sponte* amended to replace the discussion of claim 18 with the above.

Claims 1–11 and 13–24 are unpatentable under 35 U.S.C. § 103(a) over Schlegl and Hevehan.

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