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Paper 13
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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

v.

AMGEN, INC. and AMGEN MANUFACTURING, LIMITED,
Patent Owner.

Case IPR2019-00971
Patent 9,856,287 B2

Before ZHENYU YANG, J. JOHN LEE, and
CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges*.

LEE, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314(a)

INTRODUCTION

Fresenius Kabi USA, LLC and Fresenius Kabi SwissBioSim GmbH (collectively, "Fresenius") filed a Petition (Paper 3, "Pet.") requesting an *inter partes* review of claims 1, 4–6, 8–10, 12, 14–16, 19–21, 23–26, 29, and 30 ("the challenged claims") of U.S. Patent No. 9,856,287 B2 (Ex. 1001, "the '287 Patent"). Amgen Inc. and Amgen Manufacturing, Limited (collectively, "Amgen")[1] timely filed a Preliminary Response (Paper 8, "Prelim. Resp."). Fresenius filed an authorized Reply to the Preliminary Response (Paper 11, "Reply"), and Amgen filed an authorized Sur-Reply (Paper 12, "Sur-Reply").

Upon consideration of the Petition and the Preliminary Response, and in light of Board precedent, we conclude that the Petition should be denied under the discretion provided to the Director in 35 U.S.C. § 314(a).

A. Related Cases

The parties identify the following matters as related to the '287 Patent and, thus, the present case:

Amgen Inc. v. Adello Biologics LLC, No. 2:18-cv-03347 (D.N.J.)

Amgen Inc. v. Apotex Inc., No. 19-cv-61828 (S.D. Fla.)

Adello Biologics LLC v. Amgen Inc., Case PGR2019-00001 (PTAB)

Pet. 4; Paper 6, 1. The parties also note that U.S. Patent No. 8,952,138 and U.S. Patent Application Nos. 14/793,590, 14/611,037, and 15/889,559 are related or may be affected by the present case.

[1] Amgen notes that Amgen Inc. is the owner of the '287 Patent whereas Amgen Manufacturing, Limited is an exclusive licensee. Prelim. Resp. 1 n.2.

B. Background of the '287 Patent

The '287 Patent relates to a method of refolding proteins expressed in non-mammalian cells. Ex. 1001, 2:62–3:4. Such refolding is necessary in some non-mammalian expression systems, such as bacteria, "because of the inability of a bacterial host cell to fold recombinant proteins properly at high levels of expression." *Id.* at 1:25–32. As a result, the improperly-folded proteins are insoluble and precipitate out of solution to form inclusion bodies. *Id*. According to the '287 Patent, prior art refolding techniques did not demonstrate refolding of larger, more complex protein molecules at high concentrations, i.e., 2.0g/L or higher, at a scale suitable for industrial applications. *Id.* at 2:8–32.

C. Challenged Claims

Fresenius challenges claims 1, 4–6, 8–10, 12, 14–16, 19–21, 23–26, 29, and 30. Claims 1, 10, 16, and 26 are the independent claims. Claim 1 is illustrative and is reproduced below:

> 1. A method or refolding proteins expressed in a non-mammalian expression system, the method comprising:
>
> contacting the proteins with a preparation that supports the renaturation of at least one of the proteins to a biologically active form, to form a refold mixture, the preparation comprising:
>
> > at least one ingredient selected from the group consisting of a denaturant, an aggregation suppressor and a protein stabilizer;
> >
> > an amount of oxidant; and
> >
> > an amount of reductant;

> wherein the amounts of the oxidant and the reductant are related through a thiol-pair ratio and a thiol-pair buffer strength,
>
> wherein the thiol-pair ratio is in the range of 0.001-100; and
>
> wherein the thiol-pair buffer strength maintains the solubility of the preparation; and
>
> incubating the refold mixture so that at least about 25% of the proteins are properly refolded.

Ex. 1001, 18:21–41.

D. Asserted Grounds of Unpatentability and Asserted Prior Art

Fresenius challenges the patentability of claims 1, 4–6, 8–10, 12, 14–16, 19–21, 23–26, 29, and 30 of the '287 Patent on the following grounds (Pet. 23):

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1, 4, 8–10, 12, 14–16, 19, 23–26, 29, 30	102(a)(1)	Vallejo[2]
16, 19–21, 23–26, 29, 30	102(a)(1)	Ruddon[3]

[2] Eur. Patent App. No. EP 1449848 A1, published Aug. 25, 2004 (Ex. 1031, "Vallejo").

[3] PCT Int'l App. Pub. No. WO 95/32216, published Nov. 30, 1995 (Ex. 1025, "Ruddon").

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1, 4–6, 8–10, 12, 14–16, 19–21, 23–26, 29, 30	103	Ruddon, Clark 1998,[4] Schafer[5]/Gilbert 1995[6]
8, 9, 14, 15, 23–25, 30	103	Ruddon, Clark 1998, Vallejo, Schafer/Gilbert 1995

In addition, Fresenius relies on the Declaration of Paul A. Dalby, Ph.D. (Ex. 1002) in support of the asserted grounds of unpatentability.

ANALYSIS

Discretionary Denial of Petition Under § 314(a)

Amgen argues that institution of an *inter partes* review should be denied under 35 U.S.C. § 314(a) and the Board's precedents in *General Plastic Industrial Co. v. Canon Kabushiki Kaisha*, Case IPR2016-01357,

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[4] Eliana De Bernardez Clark et al., *Oxidative Renaturation of Hen Egg-White Lysozome*, BIOTECH. PROGRESS, Jan./Feb. 1998, at 47–54 (Ex. 1007, "Clark 1998").

[5] Freya Q. Schafer & Garry R. Buettner, *Redox Environment of the Cell as Viewed Through the Redox State of the Glutathione Disulfide/Glutathione Couple*, 30 FREE RADICAL BIOL. & MED. 1191–1212 (Ex. 1027, "Schafer").

[6] Hiram F. Gilbert, *Thiol/Disulfide Exchange Equilibria and Disulfide Bond Stability, in* 251 METHODS IN ENZYMOLOGY 8 (Lester Packer ed., 1995) (Ex. 1014, "Gilbert 1995"). The Petition initially indicates its reliance on Gilbert 1995 (called "Gilbert" in the Petition). *See* Pet. 48 n.9. As Amgen points out (Prelim. Resp. 53–54), however, the Petition also cites repeatedly to "Gilbert 1990," a different reference albeit by the same author. *See, e.g.*, Pet. 53. Although we do not reach the merits of Fresenius' challenges, we note that 37 C.F.R. § 42.104(b)(5) requires a petition for *inter partes* review to provide a clear statement of, *inter alia*, "[t]he exhibit number of the supporting evidence relied upon to support the challenge and the relevance of the evidence to the challenge raised."

Paper 19 (PTAB Sep. 6, 2017) (precedential as to Section II.B.4.i), and *Valve Corporation v. Electronic Scripting Products, Inc.*, Case IPR2019-00062, Paper 11, at 9 (PTAB Apr. 2, 2019) (precedential). Prelim. Resp. 23–31. Although Fresenius only briefly addressed this issue in the Petition (Pet. 3), the Reply was authorized specifically to address it, including "any relevant legal authority." *See* Paper 10, 1; Reply 3–5. The Reply, however, does not cite *General Plastic*, and it mentions *Valve* only in passing without addressing it in detail.

Institution of an *inter partes* review may be denied as a matter of discretion. *See* 35 U.S.C. § 314(a); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2140 (2016) ("[T]he agency's decision to deny a petition is a matter committed to the Patent Office's discretion."). In *General Plastic*, the Board set forth seven "non-exhaustive" factors considered when assessing whether to exercise the discretion to deny institution. *Gen. Plastic*, Paper 19, at 16. We address each factor below.

Factor 1: Previous Filed Petitions Against the Same Claims

Under *General Plastic*, we first assess "whether the same petitioner previously filed a petition directed to the same claims of the same patent." *Id*. In *Valve*, the Board expanded the scope of this factor, holding that "our application of the *General Plastic* factors is not limited solely to instances when multiple petitions are filed by the same petitioner." *Valve*, Paper 11, at 9. When, as here, "different petitioners challenge the same patent, we consider *any relationship* between those petitioners." *Id*. (emphasis added).

In *Valve*, the two petitioners at issue had filed separate petitions that each challenged the same claims of the same patent. *Id*. at 10. Further, both petitioners were co-defendants in litigation in which both were accused of

infringing that patent, and the infringement allegations involved technology that one petitioner had licensed from the other petitioner. *Id.* Consequently, the panel in *Valve* held that "[t]he complete overlap in the challenged claims and the significant relationship between [the petitioners] favor denying institution." *Id.*

Here, the Petition here and the petition filed by Adello Biologics LLC ("Adello") in PGR2019-00001 also have complete overlap in the challenged claims—the earlier-filed Adello petition challenged each of the claims of the '287 Patent now challenged in the present Petition. *See Adello Biologics LLC v. Amgen Inc.*, Case PGR2019-00001, Paper 13, at 2 (PTAB Apr. 19, 2019). Unlike the petitioners in *Valve*, Adello and Fresenius are not co-defendants, and there is no evidence indicating any business relationship between them. Fresenius admits, however, that its counsel attended the deposition of Adello's expert in PGR2019-00001. Reply 3. Moreover, Fresenius represents that "[Fresenius] and Adello are willing to coordinate this IPR with the instituted PGR . . . to facilitate joint consideration by the Board." *Id.* Thus, by its own admission, Fresenius clearly is seeking to coordinate its challenges in the present case with Adello's challenges in PGR2019-00001. On the whole, based on the precedent in *Valve* that requires we consider "any relationship" between the petitioners, we determine that these facts indicate the first *General Plastic* factor weighs in favor of denying institution.

Factor 2: Knowledge of the Prior Art

We next evaluate "whether at the time of filing of the first petition the petitioner knew of the prior art asserted in the second petition or should have known of it." *Gen. Plastic*, Paper 19, at 16. The concern in *General Plastic*

was whether the petitioner, in filing a second petition, relied on prior art that it should have asserted in the first petition because it knew, or should have known, about that prior art when filing the first petition. *See id.* at 20–21.

The scope of this factor also was expanded in *Valve*, where the panel found that the second petitioner "knew or should have known" of certain prior art asserted in its petition around the time the first petition was filed because "it was one of the two references relied upon" by the first petitioner. *Valve*, Paper 11, at 11. In other words, although the second petitioner did not file the first petition, its knowledge of the prior art asserted in that first petition at about the time it was filed weighed in favor of denial of the second petition based on the same art. *See id*.

Amgen argues that, similar to *Valve*, the present Petition relies on prior art also relied on in the earlier-filed petition in PGR2019-00001, specifically Vallejo and Ruddon. Prelim. Resp. 25–26; *see Adello*, Paper 13, at 8–9. Fresenius does not offer any argument distinguishing *Valve* with respect to this factor, nor does it dispute that it knew or should have known of Vallejo and Ruddon at about the time Adello filed the petition in PGR2019-00001. We are persuaded that the pertinent facts here are similar to those in *Valve*, and, thus, determine that the second *General Plastic* factor weighs against institution under the Board's precedents.

Factor 3: Availability of Information from Earlier Proceeding

Next, we consider "whether at the time of filing of the second petition the petitioner already received the patent owner's preliminary response to the first petition or received the Board's decision on whether to institute review in the first petition." *Gen. Plastic*, Paper 19, at 16. This factor is "directed to Petitioner's potential benefit from receiving and having the

opportunity to study Patent Owner's Preliminary Response . . . prior to its filing of follow-on petitions." *Id.* at 17.

The present Petition was filed on April 14, 2019. *See* Paper 4, 1. Thus, Fresenius did not have available our institution decision in PGR2019-00001, which was issued on April 19, 2019. Amgen's preliminary response in PGR2019-00001, however, was filed on January 23, 2019. *See Adello*, Paper 8. Thus, it was available at the time Fresenius filed the present Petition. Further, a significant portion of the arguments and contentions in the present Petition are similar to those in Adello's petition in PGR2019-00001, such as those relating to alleged anticipation by Vallejo, which supports Amgen's position that Fresenius benefited from Adello's petition and, thus, likely Amgen's preliminary response as well. *See* Prelim. Resp. 26–27; *see also id.* at 14–18 (arguing that the Petition's arguments are substantially the same as those in Adello's petition in PGR2019-00001). We conclude that this factor also weighs against institution.

Factors 4 & 5: Delay in Filing Petition

We next examine "the length of time that elapsed between the time the petitioner learned of the prior art asserted in the second petition and the filing of the second petition" (factor 4), and "whether the petitioner provides adequate explanation for the time elapsed between the filings of multiple petitions directed to the same claims of the same patent" (factor 5). *Gen. Plastic*, Paper 19, at 16. In *Valve*, these factors were held to weigh against institution because the second petitioner knew or should have known about the prior art ultimately asserted in the second petition when the first petition was filed, but waited five months before filing the second petition. *See Valve*, Paper 11, at 14. The second petitioner's interests aligned with those

of the first petitioner, and the second petitioner "could have filed its Petition at or around the same time" as the first petition. *Id*.

As discussed above, Fresenius "knew or should have known" about the prior art asserted in its Petition, particularly Vallejo and Ruddon, under the analysis in *Valve*. The Petition was filed on April 14, 2019, which was nearly three months after Amgen's preliminary response was filed in PGR2019-00001, and over six months after Adello filed its petition on October 1, 2018. *See* Paper 4, 1; *Adello*, Paper 8; *Adello*, Paper 6, 1. Although it is unclear to what extent Fresenius' and Adello's interests coincide, the presence of Fresenius' counsel at the deposition of Adello's expert in PGR2019-00001 appears to indicate they intersect. *See* Reply 3.

Further, Fresenius explains the timing of its Petition by noting that it was "not engaged in litigation over the '287 Patent and had no reason to assess invalidity positions any earlier." Reply 4. The panel in *Valve* rejected a similar explanation; the petitioner there indicated that an intervening change in law had created a need to file a petition to preserve its ability to do so, whereas it had no intention of filing any petitions under the previous law once it had been dismissed voluntarily from the infringement litigation (i.e., it was not engaged in litigation with the patent owner). *Valve*, Paper 11, at 13–14. Based on the precedent in *Valve*, we conclude that the fourth and fifth *General Plastic* factors weigh against institution.

Factors 6 & 7: Board Resources and Statutory Deadlines

Finally, we consider "the finite resources of the Board" (factor 6), and "the requirement under 35 U.S.C. § 316(a)(11) to issue a final determination not later than 1 year after the date on which the Director notices institution of review" (factor 7). *Gen. Plastic*, Paper 19, at 16. "The sixth and seventh

factors are efficiency considerations." *Valve*, Paper 11, at 15. "In general, having multiple petitions challenging the same patent, especially when not filed at or around the same time as in this case, is inefficient and tends to waste resources." *Id*. Similar to *Valve*, the present Petition was filed over six months after Adello's petition, and the resulting post-grant review was instituted less than a week after the present Petition was filed.

Although Fresenius expresses its willingness to "coordinate this IPR with the instituted PGR, including by expediting [Fresenius'] briefing and discovery" and that consideration of the present Petition in coordination with Adello's post-grant review would be more efficient (Reply 3–5), Fresenius fails to distinguish this case from the facts of *Valve*. Moreover, the post-grant review in PGR2019-00001 was instituted approximately six months ago and Amgen's patent owner response has already been filed. *See Adello*, Paper 19. Thus, coordination with the present case, even if instituted, would be impractical. While Fresenius may be correct that defending two challenges against the '237 Patent, in and of itself, is not unduly burdensome for Amgen, the sixth and seventh *General Plastic* factors concern the burden on the Board. Thus, we conclude that these factors weigh against institution.

CONCLUSION

For the foregoing reasons, based on Board precedents and the information presented in the parties' briefing, we determine that all of the *General Plastic* factors weigh against institution. As a result, we conclude

that exercising the discretion provided in 35 U.S.C. § 314(a) is warranted to deny institution of an *inter partes* review.[7]

ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* and no trial is instituted.

[7] Consequently, we do not reach the merits of Fresenius' challenges, nor do we reach the issue of whether the Petition should be denied under 35 U.S.C. § 325(d) or 35 U.S.C. § 311(c)(2).

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