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Paper 12
Entered: November 13, 2019

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PFENEX INC.,
Petitioner,

v.

GLAXOSMITHKLINE BIOLOGICALS SA,
Patent Owner.

IPR2019-01027
Patent No. 9,422,345 B2

Before SHERIDAN K. SNEDDEN, JO-ANNE M. KOKOSKI, and RICHARD J. SMITH, *Administrative Patent Judges.*

SMITH, *Administrative Patent Judge*.

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

I. INTRODUCTION

Pfenex Inc. ("Petitioner") filed a Petition to institute an *inter partes* review of claims 1, 2, 4, 6, 8, 12–14, 17–19, and 21 ("the challenged claims") of U.S. Patent No. 9,422,345 B2 (the "'345 patent") on May 6, 2019. Paper 2 ("Pet." or "'027 Petition"). GlaxoSmithKline Biologicals SA ("Patent Owner") filed a Preliminary Response to the Petition on August 16, 2019. Paper 8 ("Prelim. Resp.").

On May 6, 2019, Petitioner concurrently filed another petition for *inter partes* review of the challenged claims of the '345 patent on other grounds. *Pfenex Inc. v. GlaxoSmithKline Biologicals SA*, IPR2019-01028, Paper 2 (PTAB May 6, 2019) ("'028 Petition").[1] On August 9, 2019, Petitioner filed another petition for *inter partes* review of claims 1, 2, 4–14, and 16–21 of the '345 patent on other grounds. *Pfenex Inc. v. GlaxoSmithKline Biologicals SA*, IPR2019-01478, Paper 3 (PTAB Aug. 9, 2019) ("'478 Petition").

In connection with the '478 Petition, Petitioner also filed a paper titled "Petitioner's Explanation of Multiple Petitions Challenging Patent No. 9,422,345 and Ranking of Petitions" ("'478 Multiple Petitions Paper"). *Pfenex*, IPR2019-01478, Paper 2. The '478 Multiple Petitions Paper was filed pursuant to the Office Patent Trial Practice Guide, July 2019 Update ("TPG July 2019 Update").[2] TPG July 2019 Update, 26–28. The '478 Multiple Petitions Paper addressed the present Petition, the '028 Petition, and the '478 Petition, and included a table listing the preferred ranking of

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[1] The present Petition and '028 Petition, both filed on May 6, 2019, are referred to herein as the "Concurrent Petitions."
[2] 84 Fed. Reg. 33,925 (July 16, 2019), available at https://www.uspto.gov/TrialPracticeGuide3.

those three petitions, but was not filed in either the present case or IPR2019-01028.

On September 27, 2019, we requested a conference call with the parties to discuss the filing of a "multiple petitions" paper in both the present case and IPR2019-01028, pursuant to the TPG July 2019 Update. Ex. 3001.[3] In that e-mail, we also indicated that "[i]n lieu of a teleconference, Petitioner may file the ['478 Multiple Petitions Paper] in each of IPR2019-01027 and IPR2019-01028." *Id.* Petitioner responded via e-mail on September 30, 2019, indicating that (1) Petitioner proposed filing the '478 Multiple Petitions Paper in both the present case and IPR2019-01028, revised to update the caption for the corresponding case and adding the case number for IPR2019-01478 in the table ranking the three petitions, and (2) Patent Owner requested to file a three page response to Petitioner's multiple petitions filings, which Petitioner did not oppose in the interest of expediting the matter. *Id.* On October 2, 2019, we notified the parties via e-mail that Petitioner's proposal, as outlined in its e-mail of September 30, 2019, was acceptable. *Id.*

Thereafter, Petitioner filed a paper titled "Petitioner's Explanation of Multiple Petitions Challenging Patent No. 9,422,345 and Ranking of Petitions" in both the present case (Paper 10, "'027 Multiple Petitions Paper") and IPR2019-01028 (Paper 10, "'028 Multiple Petitions Paper").[4] In those filings, Petitioner ranked the '028 Petition first, the present Petition second, and the '478 Petition third. Paper 10, 3. Patent Owner then filed a

[3] Exhibit 3001 includes three separate e-mails, two from the Board and one from Petitioner.
[4] The '027 Multiple Petitions Paper and the '028 Multiple Petitions Paper are identical except for the different case numbers in the caption.

paper titled "Patent Owner's Response to Petitioner's Explanation of Multiple Petitions Challenging Patent No. 9,422,345 and Ranking of Petitions" in both the present case (Paper 11, "Response to '027 Multiple Petitions Paper") and IPR2019-01028 (Paper 11, "Response to '028 Multiple Petitions Paper").[5]

As set forth in the decision on institution in IPR2019-01028, an *inter partes* review of claims 1, 2, 4, 6, 8, 12–14, 17–19, and 21 of the '345 patent is instituted with respect to all grounds set forth in that Petition. *See Pfenex*, IPR2019-01028. However, for the reasons provided below and in light of the specific facts of this case, we exercise the Director's discretion under 35 U.S.C. § 314(a) and deny institution of an *inter partes* review based on the present Petition.

A. Real Parties in Interest

Petitioner identifies itself as the real party-in-interest. Pet. 3.

Patent Owner identifies itself as the real party-in-interest. Paper 4, 1.

B. Related Proceedings

Petitioner identifies the concurrently filed '028 Petition, and two petitions for *inter partes* review of the '345 patent (IPR2019-00230 and IPR2019-00241) filed by Merck Sharp & Dohme Corp. on November 7, 2018. Pet. 1.

Patent Owner identifies the following additional matters:

IPR2018-01229 and IPR2018-01236, involving U.S. Patent No. 8,753,645, and IPR2018-01234 and IPR2018-01237, involving U.S. Patent No. 9,265,839. Paper 4, 1.

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[5] The Response to '027 Multiple Petitions Paper and Response to '028 Multiple Petitions Paper are substantially identical.

C. The '345 Patent (Ex. 1001)

The '345 patent "relates to the field of the expression of bacterial toxins, in particular diphtheria toxins (including mutant forms of diphtheria toxin, such as CRM197)," and states that it "provides novel polynucleotides and polypeptides which can be used or produced during the processes of the invention." Ex. 1001, 1:9–15.

The '345 patent states that "CRM197 is a non-toxic form of the diphtheria toxin but is immunologically indistinguishable from the diphtheria toxin," and that CRM197 "differs from [diphtheria toxin] by a single base change in the structural gene . . . [leading] to a glycine to glutamine change of amino acid at position 52." *Id.* at 1:39–40, 1:44–48. CRM197 is a component in vaccines providing immunity against *Corynebacterium diphtheriae*, and has been used in vaccines as safe and effective T-cell dependent carriers for saccharides. *Id.* at 1:52–54, 1:59–61. SEQ ID NO:32 in the '345 patent is the amino acid sequence of mature[6] CRM197. *Id.* at Fig. 9E.

The '345 patent also states that the disclosed polynucleotides comprise a 5' signal sequence portion and a 3' toxin portion wherein "(a) the 5' signal sequence portion encodes a polypeptide having an amino acid sequence capable of directing transport of a heterologous protein to the bacterial periplasm and wherein the 5' signal sequence is not derived from *C. diphtheriae*;" and "(b) the 3' toxin portion encodes a polypeptide having an

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[6] The '345 patent indicates that a "mature" bacterial toxin is one in which the signal peptide has been removed. Ex. 1001, 2:37–38; 16:10–13; *see also* Ex. 1004, 570 ("'Mature' refers to a diphtheria toxin polypeptide lacking the signal sequence, see e.g. paragraphs 0153 and 0204 of the present specification.").

amino acid sequence at least 90% identical to SEQ ID NO: 32 or fragments thereof encoding at least 15 amino acids and/or at least one B or T cell epitope." *Id.* at 2:60–3:4. The '345 patent also describes various amino acid sequences of a signal peptide encoded by the 5' signal portion. *Id.* at 3:7–19.

D. Illustrative Claims

Claims 1 and 6 are the only independent claims, and are reproduced below:

> 1. A polynucleotide comprising a 5' signal sequence portion and a 3' toxin portion wherein:
>
> (a) the 3' toxin portion encodes a mature bacterial toxin polypeptide having an amino acid sequence at least 90% identical to SEQ ID NO: 32; and
>
> (b) the 5' signal sequence portion encodes a polypeptide having an amino acid sequence capable of directing transport of said bacterial toxin polypeptide to the bacterial periplasm when expressed in a ba[c]terial host cell, and wherein the 5' signal sequence is not derived from *C. diphtheriae*.

Ex. 1001, 49:54–64.

> 6. A polynucleotide comprising a 5' signal sequence portion and a 3' toxin portion, wherein:
>
> (i) the 3' toxin portion encodes a mature bacterial toxin polypeptide having an amino acid sequence at least 90% identical to SEQ ID NO:32; and
>
> (ii) the 5' signal sequence portion encodes a polypeptide having an acid sequence capable of directing transport of said bacterial toxin polypeptide to the bacterial periplasm when expressed in a bacterial host cell, and wherein the 5' signal sequence is not derived from *C. diphtheria*, and wherein the encoded polypeptide has an amino acid sequence selected from:
>
> (a) SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, and 26;
>
> (b) variants of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, or 26, varying from the corresponding sequences by 1, 2 or 3 point mutations, amino acid insertions or amino acid deletions, which variants are capable of directing transport of

> said bacterial toxin polypeptide to the periplasm of said bacterial host cell; and
>
> (c) fragments of at least 10 amino acids of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, or 26, which fragments are capable of directing transport of said bacterial toxin polypeptide to the periplasm of said bacterial host cell.

Id. at 51:13–37.

Claims 2, 4, 18, 19 and 21 depend directly from claim 1, and claims 8, 12–14, and 17 depend directly from claim 6. *See id.* at 49:65–52:42.

E. The Asserted Grounds of Unpatentability

Petitioner asserts that the challenged claims would have been unpatentable based on the following grounds. Pet. 5.

Claims Challenged	35 U.S.C. §	Reference(s)
1, 2, 18, 19, 21	102(b)	Mekada[7]
1, 2, 18, 19, 21	103(a)	Mekada and Novagen pET plasmid vector series[8]
4, 6, 8, 12, 13, 14, 17	103(a)	Mekada, Novagen pET plasmid vector series, and Thie[9]

[7] Mekada et al., India Patent Application No. 9745/DELNP/2007 A, published June 20, 2008 ("Mekada"). Ex. 1049.
[8] Novagen pET System Tutorial, Vector Cloning/Expression Regions, and Vector Maps, available at https://web.archive.org (*see* full web addresses at Pet. 8–9 (List of Exhibits)). Ex. 1043–1048.
[9] H. Thie et al., *SRP and Sec pathway leader peptides for antibody phage display and antibody fragment production in E. coli*, 25 NEW BIOTECHNOLOGY 1, 49–54 (2008). Ex. 1052.

II. DISCUSSION

A. Background

Institution of *inter partes* review is discretionary. *See* 35 U.S.C. § 314(a); *SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1356 (2018) (explaining that section "314(a) invests the Director with discretion on the question *whether* to institute review"); *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) ("[T]he PTO is permitted, but never compelled, to institute an IPR proceeding.").

The Office Patent Trial Practice Guide, August 2018 Update ("TPG August 2018 Update")[10] states

> [t]here may be other reasons besides the "follow-on" petition context where the "effect . . . on the economy, the integrity of the patent system, the efficient administration of the Office, and the ability of the Office to timely complete proceedings," 35 U.S.C. § 316(b), favors denying a petition even though some claims meet the threshold standards for institution under 35 U.S.C. §§ 314(a), 324(a). This includes, for example, events in other proceedings related to the same patent, either at the Office, in district courts, or the ITC.

Id. at 10.

The TPG July 2019 Update states that "one petition should be sufficient to challenge the claims of a patent in most situations," although "there may be circumstances in which more than one petition may be necessary." TPG July 2019 Update, 26. According to the TPG July 2019 Update, "[t]wo or more petitions filed against the same patent at or about the same time (e.g., before the first preliminary response by the patent owner) may place a substantial and unnecessary burden on the Board and the patent

[10] 83 Fed. Reg. 39,989 (August 13, 2018), available at https://go.usa.gov/xU7GP.

owner and could raise fairness, timing, and efficiency concerns." *Id.* (citing 35 U.S.C. § 316(b)).

The TPG July 2019 Update further states:

> To aid the Board in determining whether more than one petition is necessary, if a petitioner files two or more petitions challenging the same patent, then the petitioner should, in its petitions or in a separate paper filed with the petitions, identify: (1) a ranking of the petitions in the order in which it wishes the Board to consider the merits, if the Board uses its discretion to institute any of the petitions, and (2) a succinct explanation of the differences between the petitions, why the issues addressed by the differences are material, and why the Board should exercise its discretion to institute additional petitions if it identifies one petition that satisfies petitioner's burden under 35 U.S.C. § 314(a).

Id. at 27 (footnote omitted).

We have identified the '028 Petition as satisfying Petitioner's burden under 35 U.S.C. § 314(a), and institute an *inter partes* review of claims 1, 2, 4, 6, 8, 12–14, 17–19, and 21 on the grounds presented in the '028 Petition. In this case, we consider whether to exercise our discretion to deny the present Petition based on the concurrent filing of the '028 Petition.[11]

B. Analysis

As noted above, the Director has always possessed statutory discretion whether to institute an *inter partes* review based on a petition, both before and after promulgation of the Trial Practice Guide Updates of August 2018 and July 2019. *See* 35 U.S.C. § 314(a). Moreover, at least one Board panel requested the multiple petitions information identified at page 27 of the TPG

[11] Although the '027 Multiple Petitions Paper also addresses the '478 Petition, we do not address the '478 Petition in this Decision, and limit our discussion to the Concurrent Petitions.

July 2019 Update prior to the issuance thereof, and panels are permitted to authorize such papers for petitions submitted before the publication of the TPG July 2019 Update, such as the present Petition and the '028 Petition. *See Comcast Cable Commc'ns, LLC v. Rovi Guides, Inc.*, IPR2019–00232, Paper 14 at 7 (PTAB May 20, 2019); TPG July 2019 Update, 27 n.4.

At our request (Ex. 3001), Petitioner filed the '027 Multiple Petitions Paper, stating that we should consider the '028 Petition first and the '027 Petition second. Paper 10, 3. However, Petitioner also advanced several arguments in support of the assertion that we should institute on both Concurrent Petitions. *Id.* at 1–5.

Petitioner argues that it filed the Concurrent Petitions "in good faith, based on the guidance that was available at the time," and that those two petitions "should not be subject to the new guidance" in the TPG July 2019 Update. Paper 10, 1–2 (citing *Intel Corp. v. Qualcomm, Inc.*, IPR2018-01344, Paper 8, 18 (PTAB Jan. 23, 2019) (footnote omitted)); TPG July 2019 Update, 26–28. Thus, according to Petitioner, because the Concurrent Petitions "were filed before the [TPG July 2019 Update] was issued, following guidance that was available at that time," the '027 Petition and the '028 Petition "at a minimum, should be on equal footing. . . . [and the] institution decision in those proceedings should be . . . based on the merits." Paper 10, 3.

We find these arguments unpersuasive. The issue is not the "good faith" of Petitioner in filing the Concurrent Petitions, but rather the Director's statutory discretion whether to institute an *inter partes* review, including in cases involving the concurrent filing of two or more petitions against the same claims of the same patent. *See* 35 U.S.C. § 314(a); *Comcast*, Paper 14. The TPG August 2018 Update made clear that reasons

favoring denying a petition were not limited to the "follow-on" petition context. TPG August 2018 Update, 10–11. Moreover, in the present case, Petitioner was given the opportunity to address (and did address) the two Concurrent Petitions in light of the TPG July 2019 Update. Ex. 3001; Paper 10.

Petitioner's '027 Multiple Petitions Paper describes the differences between the '027 Petition and the '028 Petition, and the reasons for filing them. Paper 10, 4–5. Petitioner states that the '028 Petition and the '027 Petition "rely on different prior art to demonstrate the unpatentability of the '345 claims." *Id.* at 4. Petitioner states that "[t]he Davis[12] and Zhou[13] references relied upon in the ['028 Petition] each relate to diphtheria toxin mutants, in particular, CRM197, while Inouye[14] and Ikemura[15] are relied upon for teaching a vector that directs the export of the mutant proteins into the periplasmic space of *E. coli*." *Id.* Petitioner further states that "in contrast, [the '027 Petition] relies on [Mekada], an Indian patent application, as an anticipatory reference, which discloses the use of CRM197 in the treatment of cancer." *Id.* As to the obviousness challenges in the '027 Petition, Petitioner "relies on Novagen pET Plasmid Vector Maps, archived by the WayBack Machine, which present vector maps that encode a signal

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[12] Davis et al., U.S. Patent Application Publication No. 2009/0010966 A1, published Jan. 8, 2009 ("Davis"). Ex. 1005.
[13] J. Zhou, *Secretory Expression of Recombinant Diphtheria Toxin Mutants in B. Subtilis*, 19 J. TONGJI MED. UNIV. 4, 253–56 (1999) ("Zhou"). Ex. 1007.
[14] S. Inouye et al., *Up promoter mutations in the lpp gene of Escherichia coli*, 13 NUCLEIC ACIDS RESEARCH 9, 3101–10 (1985) ("Inouye"). Ex. 1006.
[15] H. Ikemura et al., *Requirement of Pro-sequence for the Production of Active Subtilisin E in Escherichia coli*, 262 J. BIOL. CHEM. 16, 7859–64 (1987) ("Ikemura"). Ex. 1008.

peptide for potential periplasmic location." *Id.* Petitioner also states that it filed the "two petitions to obtain additional word count as well as to avoid potential issues presented by *SAS*." *Id.* at 5.

The Concurrent Petitions were filed by the *same* Petitioner and challenge the *same* claims of the *same* patent, i.e., the '345 patent. *See* Paper 2; *Pfenex*, IPR2019-01028, Paper 2. Moreover, we do not find the asserted differences between the '028 Petition and '027 Petition, as explained by Petitioner, to be sufficiently material to outweigh the inefficiencies and costs to the Board and Patent Owner that would result from instituting on both the '027 Petition and the '028 Petition. *See* TPG July 2019 Update, 26 ("Two or more petitions filed against the same patent at or about the same time . . . may place a substantial and unnecessary burden on the Board and the patent owner and could raise fairness, timing, and efficiency concerns.").

The '028 Petition advances two obviousness challenges that rely on art regarding CRM197 and art regarding "a vector that directs the export of the mutant proteins into the periplasmic space." Paper 10, 4. Although the '027 Petition advances an anticipatory challenge based on Mekada, Petitioner relies on Mekada for its teachings of CRM197, similar to its reliance on Davis and Zhou in the '028 Petition. *Id.* As for the signal peptide "capable of directing transport of said bacterial toxin polypeptide to the bacterial periplasm," Petitioner points to the disclosure of expression vector pET-22b in Mekada to argue that "the periplasmic secretion function of pET-22b is an inherent property, regardless of whether this function is discussed in Mekada." Pet. 26–27. Petitioner characterizes its two obviousness challenges in the '027 Petition as relying on Mekada and art "which present[s] vector maps that encode a signal peptide for potential

periplasmic location," similar to Petitioner's reliance on Inouye and Ikemura for "a vector that directs the export of the mutant proteins into the periplasmic space" in the '028 Petition. Paper 10, 4. We thus agree with Patent Owner that "the redundancy of Petitioner's references and the similar manner in which Petitioner relies on them is evident from Petitioner's own characterization of their teachings." Paper 11, 2.

Although Petitioner describes some differences between the '028 Petition and '027 Petition, it fails to persuasively explain "why the issues addressed by the differences are material." TPG July 2019 Update, 27. We are not persuaded on this record that merely arguing that different art is cited, or that the '027 Petition includes an anticipation challenge, explains "why the issues addressed by the differences are material." *See id.*; Paper 10, 4.

Petitioner states that it filed the Concurrent Petitions "to obtain additional word count as well as to avoid potential issues presented by *SAS*." Paper 10, 5. But Petitioner does not explain a compelling need for "additional word count," such as (for example) "when the patent owner has asserted a large number of claims in litigation or when there is a dispute about priority date requiring arguments under multiple prior art references." TPG July 2019 Update, 26. Petitioner does not identify its involvement in any litigation regarding the '345 patent, only challenges twelve claims (including only two (similar) independent claims), and addresses the same claim construction issue in a few pages in both the '027 Petition and the '028 Petition. *See* Pet. 1, 11–13; Ex. 1001, 49:54–64, 51:13–37; *Pfenex*, IPR2019-01028, Paper 2 at 11–13. In short, the mere fact that Petitioner may have had additional art to assert, including a different statutory basis for asserting that art, does not, on these facts, justify the additional burden of a

second petition directed to the same claims. *See* Prelim. Resp. 17 ("Petitioner failed to provide sufficient explanation as to why this case presents an exceptional circumstance in which more than a single petition is necessary.").

Nor does Petitioner explain the "potential issues presented by *SAS*" that it alleges it sought to avoid with two petitions rather than one. Paper 10, 5. Petitioner does not explain, for example, whether (and if so, why) it was concerned that the Board might deny institution if all five of its challenges were included in one petition.

Patent Owner argues that, as between the '027 Petition and the '028 Petition, we should exercise our discretion to deny institution of the '028 Petition because "the obviousness grounds raised in the ['028 Petition] are duplicative and cumulative of those raised in the ['027 Petition]." Paper 11, 3. Assuming for the sake of argument that Patent Owner's argument has merit, the obviousness grounds in the '027 Petition would also be duplicative and cumulative of the obviousness grounds in the '028 Petition. Here, Petitioner ranked the '028 Petition ahead of the '027 Petition, and Patent Owner has not persuasively shown why we should disregard Petitioner's preference and proceed with the '027 Petition rather than the '028 Petition. *See Comcast*, Paper 14 at 12–13 (instituting on Petitioner's preferred petition).

Accordingly, we institute an *inter partes* review on all grounds presented in the '028 Petition (*see* IPR2019-01028), and exercise the Director's discretion under 35 U.S.C. § 314(a) to deny institution of the present Petition.

III. ORDER

Accordingly, it is

ORDERED that Petitioner's request for an *inter partes* review of claims 1, 2, 4, 6, 8, 12–14, 17–19, and 21 of the '345 patent is *denied* and no *inter partes* review is instituted.

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