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Paper No. 22
Date: February 5, 2020

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NOF CORPORATION,
Petitioner,

v.

NEKTAR THERAPEUTICS,
Patent Owner.

IPR2019-01394
Patent 7,026,440 B2

Before ERICA A. FRANKLIN, ZHENYU YANG, and JON B. TORNQUIST, *Administrative Patent Judges*.

TORNQUIST, *Administrative Patent Judge*.

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

PUBLIC VERSION

[redacted]

INTRODUCTION

NOF Corporation ("Petitioner") filed a Petition (Paper 1, "Pet.") requesting an *inter partes* review of claims 1–20 and 29–35 of U.S. Patent No. 7,026,440 B2 (Ex. 1001, "the '440 patent"). Nektar Therapeutics ("Patent Owner") filed a Preliminary Response (Paper 8, "Prelim. Resp."). With Board authorization, Petitioner filed a Reply to the Preliminary Response (Paper 17, "Reply") and Patent Owner filed a Sur-reply (Paper 19). [1][2]

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314 (2012); 37 C.F.R. § 42.4(a) (2019). The standard for institution is set forth in 35 U.S.C. § 314(a), which provides that an *inter partes* review may not be instituted "unless the Director determines . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition."

After considering the parties' arguments and evidence, we determine that Petitioner has demonstrated a reasonable likelihood that it would prevail with respect to at least one challenged claim of the '440 patent. Accordingly, we institute an *inter partes* review as to all challenged claims on all asserted grounds.

A. Related Matters

Petitioner identifies *Nektar Therapeutics et al. v. Bayer Healthcare, LLC*, 1-18-cv-01355 (D. Del. August, 31, 2018) as a related matter. Pet. 2.

[1] The Preliminary Response, Reply, and Sur-reply were filed under seal. Paper 8; Paper 17; Paper 19. The parties provide redacted versions of each paper in the record. Paper 15; Paper 18; Paper 20.
[2] The Reply and Sur-reply are limited to addressing whether a non-party is a real party in interest.

In contrast, Patent Owner identifies *Baxalta Incorporated v. Bayer Healthcare LLC*, No. 17-1316 (D. Del) (consolidated) as a related matter. Paper 6, 1.

B. The '440 Patent

The '440 patent discloses "branched, reactive water soluble polymers useful for conjugating to biologically active molecules" and "methods for making and utilizing such polymers." Ex. 1001, 1:15–18. The '440 patent explains that it was known in the art that covalent attachment of hydrophilic polymer poly(ethylene glycol), or PEG, may increase water solubility and bioavailability of biologically active molecules, particularly hydrophobic molecules. *Id*. at 1:22–30 (citing Greenwald, et al., *J. Org. Chem.*, 60:331–336 (1995)). The total molecular weight of the attached polymers is chosen to provide the advantageous characteristics typically associated with PEG polymer attachment, while at the same time avoiding "adversely impacting the bioactivity of the parent molecule." *Id*. at 1:30–35.

The '440 discloses that methods for forming branched polymers attached to a central core and having a single reactive group for conjugation to a biologically active molecule were known in the art, but required "extensive purification of the PEG polymers prior to attachment to the core molecule" and removal of "partially pegylated polymer intermediates." *Id*. at 1:55–2:3. Thus, according to the '440 patent, there remained a need in the art for branched polymer reagents that "provide the benefits associated with branched polymers (i.e., high overall molecular weight in a single non-linear polymer molecule), but are easier to synthesize or provide more flexibility in their design than prior art reagents." *Id*. at 2:4–9.

The '440 patent instructs that the "branched reactive polymer of the invention will typically comprise at least two water-soluble and non-peptidic polymer arms, such as poly(ethylene glycol) arms, covalently attached to an aliphatic hydrocarbon core structure bearing a single functional group." *Id.* at 7:18–22. "Typically, the total number average molecular weight of the branched reactive polymers of the invention will be about 500 to about 100,000 daltons (Da), preferably about 5,000 to about 60,000 Da, most preferably about 8,000 to about 40,000 Da." *Id.* at 7:4–8. "Unless otherwise noted" in the '440 patent, molecular weight is expressed "as number average molecular weight (M_n), which is defined $\frac{\Sigma NiMi}{\Sigma Ni}$, wherein N_i is the number of polymer molecules (or the number of moles of those molecules) having molecular weight M_i." *Id.* at 4:51–62.

C. Illustrative Claim

Claim 1 is illustrative of the challenged claims and is reproduced below:

1. A branched reactive polymer having the structure:

Y—(X)p-R(—X′-POLY)$_q$

wherein:

R is an aliphatic hydrocarbon having a length of at least three carbon atoms;

each POLY is a water soluble and non-peptide polymer, wherein the molecular weight of each POLY is selected such that the total molecular weight or the branched reactive polymer is independently selected from the group consisting of poly(alkylene glycol), poly(oxyethylated polyol), poly(olefinic alcohol), poly(vinylpyrrolidone), poly(hydroxyalkylmethacrylamide), poly(hydroxyalkylmethacrylate), polysaccharides, poly(α-

hydroxy acid), poly(vinyl alcohol), plyphosphazene, polyoxazoline, poly(N-acryloylmorpholine), and copolymers, terpolymers, and mixtures thereof is at least about 5,000 Da;

X′ is a heteroatom linkage;

X is a linker;

p is 0 or 1; q is 2 to about 10; and

Y is a functional group reactive with an electrophilic or nucleophilic group.

Ex. 1001, 24:7–30.

D. Prior Art and Asserted Grounds

Petitioner contends claims 1–20 and 29–35 of the '440 patent would have been unpatentable on the following grounds:

Claims Challenged	35 U.S.C. §	Reference(s)/Basis
1–16, 19, 20, 29–35	103	Bentley,[3]
16–18, 30	103	Bentley, Liebigs[4]
1–3, 5, 7–10, 12–16, 20, 29–35	103	Harris[5]
29, 31	102(b)	Harris
1–15, 17, 19, 20, 29, 31–33, 35	103	JP-542[6]
1–15, 17, 19, 20, 29, 31–35	103	JP-542, MDD[7]
16–18, 30	103	JP-542, Bentley

[3] Bentley, US 5,990,237, issued November 23, 1999 (Ex. 1015) ("Bentley").
[4] Edwin Weber, *Neutral ligands with surfactant structure – Synthesis, Complexation, Ion Transfer*, Liebigs Ann. Chem., 770–801, 1983 (Ex. 1019) ("Liebigs").
[5] Harris, US 5,932,462, issued August 3, 1999 (Ex. 1016) ("Harris").
[6] Sanchika, et al., JP P2000-1542A, published January 7, 2000 (Ex. 1017) ("JP-542").
[7] Steven A. Charles, et al., *Improving Hepatitis C Therapy*, Modern Drug Discovery, September 2000 (Ex. 1029) ("MDD").

Petitioner relies on the testimony of Dr. Yuji Yamamoto to support its unpatentability arguments. Ex. 1083.

ANALYSIS

A. Level of Ordinary Skill in the Art

Petitioner contends a person of ordinary skill in the art would have had a Ph.D. in Chemistry, Biochemistry, Materials Science, or a related field and 3–5 years of experience working in the field of synthesis of active PEG polymers for PEGylation of biological molecules. Pet. 12 (citing Ex. 1083 ¶¶ 45–48). Patent Owner does not address Petitioner's definition of one of ordinary skill in the art or provide its own proposed definition.

Because Petitioner's definition of one of ordinary skill in the art is reasonable and consistent with the '440 patent and the prior art of record, we adopt Petitioner's definition for purposes of this decision.

B. Claim Construction

In this proceeding, the claims of the '440 patent are construed "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b)." 37 C.F.R. § 42.100(b). Under that standard, the words of a claim are generally given their "ordinary and customary meaning," which is the meaning the term would have to a person of ordinary skill at the time of the invention, in the context of the entire patent including the specification. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

Petitioner construes the terms "aliphatic hydrocarbon" and "functional group." Pet. 11. Patent Owner disputes Petitioner's construction of the term "functional group," but does not provide a proposed definition for this term. Prelim. Resp. 12 (asserting the "plain and ordinary meaning" applies). We

address the parties' dispute with respect to the term "functional group" in our analysis of the grounds based on Harris and determine that no other claim terms are in need of construction for purposes of this decision. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy.")).

C. Real Parties in Interest

Petitioner identifies NOF Corporation and NOF America Corporation as real parties in interest, and contends "[n]o other party is a real party-in-interest or a privy of NOF CORPORATION for this Petition." Pet. 2. Patent Owner contends Bayer Healthcare LLC ("Bayer") is also a real party in interest in this case and that the Petition should not be given a filing date until all real parties in interest are identified. Prelim. Resp. 13. And because Bayer was served with a complaint more than one year from the current date, Patent Owner contends the Petition should dismissed as time barred pursuant to 35 U.S.C. § 315(b). *Id*. at 13, 16.

A petition will be accorded a filing date, and may be considered only if, it "identifies all real parties in interest." 35 U.S.C. § 312(a)(2); 37 C.F.R. § 42.106, 42.104, 42.8(b)(1); *Proppant Express Inv., LLC v. Oren Techs., LLC*, IPR2017-01917, Paper 86 at 6 (PTAB Feb. 13, 2019) (precedential). The core functions of the real party in interest requirement are to "assist members of the Board in identifying potential conflicts" "and to assure proper application of the statutory estoppel provisions." Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,759 (Aug. 14, 2012);

[redacted]

see also Consolidated Trial Practice Guide 12 (Nov. 2019) (consolidating prior Trial Practice Guide and updates).[8] The statutory estoppel provisions in turn seek "to protect patent owners from harassment via successive petitions by the same or related parties, to prevent parties from having a 'second bite at the apple,' and to protect the integrity of both the USPTO and Federal Courts by assuring that all issues are promptly raised and vetted." Office Patent Trial Practice Guide, 77 Fed. Reg. at 48,759; *see also* Consolidated Trial Practice Guide, 12–13.

The question of whether a non-party is a real party in interest is a "highly fact-dependent question" and must be considered on a case-by-case basis. *Ventex Co. v. Columbia Sportswear North America, Inc.*, IPR2017-00651, Paper 148 at 6 (PTAB Jan. 24, 2019) (precedential) (citing Office Trial Practice Guide, 77 Fed. Reg. at 48,759). Petitioner bears the ultimate burden to establish that all real parties in interest are identified in the Petition. *See Worlds Inc. v. Bungie, Inc.*, 903 F.3d 1237, 1242 (Fed. Cir. 2018); *Applications in Internet Time, LLC v. RPX Corp.*, 897 F.3d 1336, 1356 (Fed. Cir. 2018) ("AIT").

To determine whether Bayer is a real party in interest in this case we must probe (1) whether Bayer's has an interest in and will benefit from Petitioner's actions and (2) whether Petitioner can be said to be representing Bayer's interest or acting as a proxy for Bayer. *AIT*, 897 F.3d at 1353. Although there are many factors relevant to whether a non-party is a real party in interest or privy, important inquiries are "whether the non-party exercised or could have exercised control over a party's participation in a

[8] Available at https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf?MURL=

proceeding," whether the non-party funds and directs the *inter partes* review proceeding, and whether the petition was filed at the behest of a non-party.[9] Office Patent Trial Practice Guide, 77 Fed. Reg. at 48,759–60; *see also* Consolidated Trial Practice Guide, 14, 16–17.

1. Patent Owner's Arguments

Patent Owner contends Petitioner's and Bayer's interests are closely aligned, as demonstrated by the fact that (1) Petitioner and Bayer have had a well-established relationship for over 11 years; [redacted] (3) Bayer was served with a complaint asserting Jivi infringes the '440 patent; [redacted] Prelim. Resp. 15–16 (citing Ex. 2002, 26–27, 29 (Bayer Supply Agreement); Ex. 2003 (district court complaint); Ex. 2004).

Patent Owner contends the facts of this case closely mirror those in *Ventex* and demonstrate both that there is a specially structured, preexisting, and well-established business relationship between Bayer and Petitioner and

[9] Patent Owner contends an RPI is one that "is a clear beneficiary that has a preexisting, established relationship with the petitioner." Prelim. Resp. 14 (quoting *Ventex*, Paper 152 at 6). This broad statement is true, but *AIT* clarifies that the relationship must be of such a nature that it may be said that petitioner is representing the non-party's interests or that the petition was filed at the non-party's "behest." *AIT*, 897 F.3d at 1351 (quoting with approval the Trial Practice Guide's inquiry into whether the "petition has been filed at a nonparty's 'behest'"), 1353 (explaining that the relevant inquiries are whether a non-party "has an interest in and will benefit from" a petitioner's actions and whether the petitioner "can be said to be representing" the non-party's interests).

[redacted]

that any determination of invalidity as to the challenged claims would "inure to the benefit" of Bayer in the Jivi litigation. *Id*. at 16. Thus, Patent Owner contends Bayer is a real party in interest in this case.

2. Petitioner's Arguments

Petitioner argues that Bayer is not a real party in interest in this IPR because (1) Bayer was not time barred when the Petition was filed and could have filed its own petitions at that time (Reply 2–3); (2) Bayer has no ability to direct or control this IPR (*id*. at 3–4 (citing Ex. 2016))[10]; (3) Bayer did not fund, prepare, edit, review, approve, or file the Petition (*id*.); [redacted] and (5) there is no exclusivity agreement that would prevent Petitioner from selling PEG products to other parties (*id*. at 6 (citing Ex. 2016, 4; Ex. 2002, 35)). [redacted]

3. Analysis

a) Bayer Has an Interest in Petitioner's Actions

Petitioner and Bayer have a longstanding business relationship [redacted] This evidence sufficiently demonstrates that both Petitioner and Bayer have an interest in, and will benefit from, Petitioner's actions in this IPR.

[10] An unredacted version of Exhibit 2016 is available at Paper 12.

[redacted]

b) Whether Petitioner Is Representing Bayer's Interest or Filed the Petition at Bayer's Behest

The evidence of record does not suggest that Petitioner is representing Bayer's interest in this IPR or that Petitioner filed the Petition at Bayer's behest. First, neither Petitioner nor Bayer was time barred under 35 U.S.C. § 315(b) when the Petition was filed. *See* 35 U.S.C. § 315(b). This is an important factor, as there was no need for Petitioner to file the Petition at the behest of Bayer; Bayer could have just filed its own IPR if it so desired. *Ventex*, Paper 148 at 8 ("Importantly, Ventex seeks relief in this forum that Serius is barred under § 315(b) from seeking for itself."); *Puzhen Life USA, LLC v. ESIP Series 2, LLC*, IPR2017-02197, Paper 24 at 13 (PTAB Feb. 27, 2019) (declining to find an RPI relationship when there was "no evidence that [a non-party] has achieved any clear benefit from Petitioner filing the Petition that [the non-party] would not have achieved by filing and litigating the Petition itself").

Patent Owner contends Petitioner is acting as a proxy for Bayer in order to avoid the estoppel effects of this proceeding, i.e., to provide the parties with two bites at the apple. Prelim. Resp. 21–22. We note, however, that estoppel also applies to parties in privity with Petitioner, which is a more expansive concept. Office Patent Trial Practice Guide, 77 Fed. Reg. at 48,759 ("The notion of 'privity' is more expansive, encompassing parties that do not necessarily need to be identified in the petition as a 'real party-in-interest.'"); *see also* Consolidated Trial Practice Guide, 14. Thus, failure to name Bayer as an RPI does not preclude the application of estoppel in the

[redacted]

district court, nor does it necessarily suggest that the Petition was filed at the behest of Bayer in order to avoid estoppel.[11]

Second, there is no evidence that Bayer directed or controlled the filing of the Petition. Reply 3–4; Ex. 2016, 3–6. Nor is there any evidence to suggest that Bayer is directly or indirectly funding, or is otherwise involved in any way with, the current IPR proceedings. Ex. 2016, 3–6. This again is consistent with a conclusion that Petitioner is not representing Bayer's interests in this proceeding.

[redacted] there is no evidence that Bayer has the right to control the filing of the current Petition. [redacted] unlike the petitioner in *Ventex*, here Petitioner is free to provide its product (PEG) to other customers. Thus,

[11] We need not determine for purposes of this decision whether Bayer is a privy of Petitioner because Patent Owner does not allege that such a relationship would bar this proceeding.

[redacted]

Petitioner has an interest in seeing the challenged claims invalidated apart from its financial interest in Bayer's Jivi product.[12] Reply 6.

In summary, the current record suggests Petitioner and Bayer have a continuing relationship and that both parties would benefit from invalidation of the challenged claims. There is insufficient evidence, however, to suggest that Petitioner is representing Bayer's interests in this proceeding or that the Petition was filed at Bayer's behest. Thus, we are not persuaded that Bayer is an RPI or that the identification of RPIs in the Petition needs to be amended.

c) We Would Allow Petitioner to Amend its RPI Designations

The requirement to name all RPIs is not jurisdictional and a petitioner may amend its identification of real parties in interest while maintaining the original filing date under certain circumstances. *Proppant*, Paper 86 at 6–7. Factors considered in determining whether a petitioner should be allowed to amend its identification of real parties in interest include whether there have been "(1) attempts to circumvent the § 315(b) bar or estoppel rules, (2) bad faith by the petitioner, (3) prejudice to the patent owner caused by the delay, or (4) gamesmanship by the petitioner." *Id*. Patent Owner contends

[12] *AIT* states that the "point is not to probe [Petitioner's] interest" as "it does not need any." *AIT*, 897 F.3d at 1353. We do not understand this to mean that a petitioner's independent reasons for filing a petition are irrelevant to the RPI inquiry, only that a petitioner's independent reasons for filing a petition do not necessarily resolve the question of whether a third party also has an interest in the filing of the petition. *See id*. at 1354 (discussing with approval a Board decision in which it was determined that a party "had failed to explain adequately what 'independent reason' it had to file the IPR petition").

[redacted]

evaluation of the *Proppant* factors as a whole favors denying Petitioner the right to amend its identification of RPIs. Prelim. Resp. 16–17.

(1) Attempts to Circumvent § 315(b) Bar or Estoppel Rules

Neither Bayer nor Petitioner was barred under § 315(b) when the Petition was filed. Pet. 81 (Petition filed July 25, 2019); Ex. 2003 (complaint dated August 31, 2018). Accordingly, there was no attempt to circumvent the § 315(b) time bar.

Patent Owner contends that by omitting Bayer as a real party in interest, Petitioner and Bayer are attempting to evade estoppel under 35 U.S.C. § 315(e)(2). Prelim. Resp. 21–22. As noted above, however, Petitioner reasonably chose to omit Bayer from its identification of real parties in interest and its failure to name Bayer does not necessarily allow Bayer to avoid estoppel under 35 U.S.C. § 315(e)(2). Thus, there is insufficient evidence to conclude that the Petition was filed to circumvent the § 315(b) time bar or to otherwise avoid estoppel.

(2) Gamesmanship and Bad Faith

Patent Owner contends Petitioner had no good faith reason to withhold the Bayer Agreement from the Board and that Petitioner should have provided this document with its Petition. Prelim. Resp. 17–18. Patent Owner further contends that Petitioner refused to acknowledge the parties' agreement or produce it during the course of this proceeding, and Bayer actively thwarted Patent Owner's attempts to provide the parties' agreement to the Board. *Id*. at 18–19.

The Petition affirmatively states that "[n]o other party is a real party-in-interest or a privy of NOF CORPORATION for this Petition." Pet. 2. The Bayer Agreement is highly relevant to both the real party in interest and

[redacted]

privity questions. Ex. 2006, 2. Although we determine on the present evidentiary record that Bayer is not a real party in interest, the question of whether Bayer is a privy is a closer question and Petitioner made an affirmative statement in the Petition about privity. 37 C.F.R. § 42.51 (b)(1)(iii) (requiring service of "relevant information that is inconsistent with a position advanced by the party during the proceeding"). That said, the question of whether there is a privity relationship between Petitioner and Bayer is not currently before us. Thus, any potential gamesmanship is not directed to the issue of real parties in interest.

Petitioner filed a "Voluntary Interrogatory Response" in which it presented itself with interrogatory questions regarding the RPI issue and then responded to them. Ex. 2016. Patent Owner contends the filing of this exhibit is further evidence of gamesmanship. Prelim. Resp. 20–21. The filing of voluntary interrogatory responses is unusual. We do not agree, however, that Petitioner's attempt to explain to Patent Owner the relationship between Bayer and this proceeding in such an unorthodox manner constitutes gamesmanship.

(3) Prejudice to Patent Owner

Patent Owner contends it was prejudiced by Petitioner's failure to name Bayer as a real party in interest because if Bayer had been properly named Patent Owner could have directed the district court's attention to the parties' inconsistent claim construction arguments regarding the term "aliphatic hydrocarbon." Prelim. Resp. 21.

We are not persuaded by this argument because the alleged prejudice occurred in another proceeding in another forum and involved a claim construction dispute that is not before us in this proceeding. *See* Pet. 11

(construing "aliphatic hydrocarbon"); Prelim. Resp. 12 (Patent Owner not disputing Petitioner's construction); *Proppant*, Paper 86 at 10 ("First, the alleged prejudice occurred in another proceeding in another forum involving breach of contract claims that are not before us.").

(4) Conclusion

On this record, we determine that even if Petitioner was incorrect in failing to name Bayer as a real party in interest its failure to do so was not unreasonable. We also determine that consideration of the *Proppant* factors does not support preventing Petitioner from updating its identification of the real parties in interest in this proceeding.

D. Obviousness of Claims 1–16, 19, 20, 29–35 over Bentley

Petitioner contends the subject matter of claims 1–16, 19, 20, 29–35 of the '440 patent would have been obvious over the disclosures of Bentley. Pet. 17–31.

1. Bentley

Bentley discloses a method of coupling a poly(ethylene glycol) polymer to a biomaterial. Ex. 1015, 1:8–11. Bentley explains that both linear and branched PEG molecules had been used in the art to improve the solubility of "water insoluble compounds" without altering the compound's biological activity. *Id*. at 1:60–2:1. Bentley further explains that conjugation of PEG to a drug molecule may provide enhanced blood circulation lifetime due to reduced kidney clearance and reduced immunogenicity. *Id*. at 2:6–11.

Bentley discloses that conjugation of PEG to a drug molecule requires the use of an activated derivative "having a functional group at the terminus suitable for reaction with a group on the other molecule." *Id*. at 2:12–15.

[redacted]

For example, a hydroxyl group on the PEG compound can be converted to an aldehyde group and then this aldehyde group covalently linked to an amine group on a target molecule in a process called reductive amination. *Id*. at 2:15–20.

Bentley indicates that one problem reported in the art with respect to the use of PEG acetaldehyde is its high reactivity, "which leads to condensation side reactions." *Id*. at 2:42–45. Bentley also reports that PEG acetaldehyde is "difficult to prepare in high purity," requiring additional purification steps that result in the "loss of valuable bioactive molecules, such as proteins." *Id*. at 2:46–54. To overcome these difficulties, Bentley discloses the use of activated PEG molecules having an aldehyde hydrate moiety. *Id*. at 3:3–10. According to Bentley, the use of an aldehyde hydrate moiety to conjugate PEG to a target molecule avoids the condensation and oxidation reactions that hindered prior art conjugation methods. *Id*. at 3:9–15.

The activated PEG polymer of Bentley may be linear or branched and typically has an average molecular weight of from 200 to 100,000. *Id*. at 6:35–36. As biological properties may vary based on molecular weight and the degree of branching, Bentley discloses that "not all" of the disclosed derivatives "may be useful for biological or biotechnical applications." *Id*. at 6:35–39.

Bentley reports that "[f]or many biological and biotechnical applications, substantially linear, straight-chain PEG acetaldehyde hydrate is useful." *Id*. at 6:40–42. This linear PEG may be capped on one end with a relatively nonreactive moiety, such as methyl, benzyl and aryl moieties, and conjugated to either a "surface" or a "substance" "selected from, e.g.,

proteins, peptides, oligonucleotides, polysaccharides and small drug molecules." *Id*. at 6:12–15, 6:44–52, 7:44–46. According to Bentley, "[b]roadly speaking, any material having a reactive amine group accessible to the activated polymer having an aldehyde hydrate group can be used in the present invention." *Id*. at 6:15–18.

"Another form of activated PEG aldehyde is dendritic activated PEG in which multiple arms of PEG are attached to a central core structure." *Id*. at 6:64–66. These dendritic PEGs are commonly known as "star" molecules and can be represented by the formula $Q[poly]_y$, wherein Q is a branching core moiety and y is from 2 to about 100. *Id*. at 6:66–7:6. Bentley notes that such "star" molecules are generally described in Merrill (U.S. Patent No. 5,171,264), which is incorporated by reference in Bentley. *Id*. at 7:5–8.

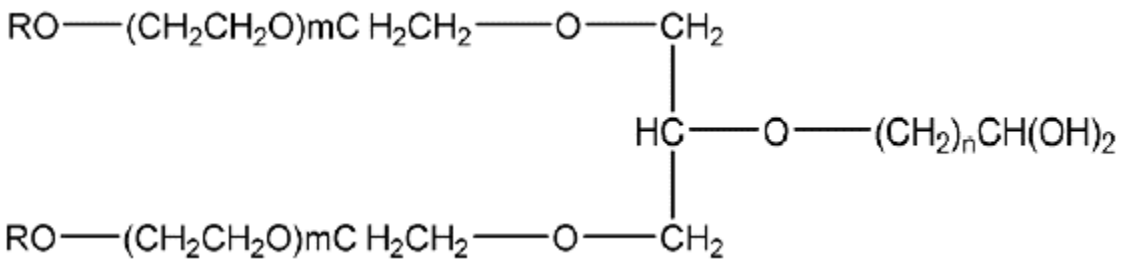
Bentley discloses that the aldehyde hydrate moiety on the "star" molecules can be used to provide an active, functional group on the end of the PEG chain extending from the core, or may act as a linker for joining a functional group to the star molecule arms. *Id*. at 7:8–12.

> Additionally, the aldehyde hydrate moiety can also be linked directly to the core molecule having PEG chains extending from the core. One example of such a dendritic activated PEG has a formula of $[RO–(CH_2CH_2O)_mCH_2CH_2–O–CH_2]_2CH–O–(CH_2)_nCH(OH)_2$ wherein R is H, alkyl, benzyl, or aryl; m ranges from about 5 to about 3000, [and] n ranges from 1 to 6.

Id. at 7:12–20.

2. Analysis of Claim 1

Petitioner contends the dendritic "star" molecule of Bentley identified above may be drawn as follows:



Pet. 18. The figure above is Petitioner's depiction of the chemical structure identified at column 7, lines 16–20 of Bentley. *Id*. (citing Ex. 1015, 7:12–20).

Petitioner asserts the dendritic molecule of Bentley expressly discloses every limitation of claim 1 of the '440 patent, except a molecular weight of "at least about 5,000 Da." *Id*. at 18–19. Petitioner notes, however, that Bentley instructs that "m" may range from about 5 to about 3000, which Dr. Yamamoto testifies describes a molecular weight range of "at least 440 to about 264,000 Da for the branched reactive polymers." *Id*. at 18 (citing Ex. 1015, 7:12–20, 14:59–65; Ex. 1083 ¶¶ 305–306). As this range overlaps the range set forth in claim 1, Petitioner contends the claimed range is *prima facie* obvious. *Id*. at 19 (citing *In re Peterson*, 315 F.3d 1325, 1329-30 (Fed. Cir. 2003)).

Petitioner contends one of ordinary skill in the art would have had a reasonable expectation of success in preparing a branched polymer with a molecular weight of "at least about 5,000 Da" because this range overlaps with the range expressly disclosed in Bentley and because polymerization or substitution of larger PEG chains was known in the art. *Id*. (citing Ex. 1015, 1:14–47, Claim 21; Ex. 1083 ¶ 308; Ex. 1017; Ex. 1016).

Patent Owner contends the broad molecular weight ranges of Bentley would not have invited routine optimization. Prelim. Resp. 33–34 (citing *Peterson*, 315 F.3d at 1330 n.1). We are not persuaded by this argument because there is no evidence that one of ordinary skill in the art would have considered this range to be "very broad." Moreover, to the extent Bentley's disclosed range is considered "very broad," it is still more limited in scope than the claimed range, which allows any molecular weight above 5,000 Da.

Patent Owner also contends that Petitioner has failed to explain why one of ordinary skill in the art would have selected the dendritic polymer of Bentley over all other polymers disclosed in the reference.
Prelim. Resp. 29–30. We are not persuaded by this argument because Bentley provides a single, consolidated disclosure that teaches or suggests every limitation of claim 1 and Bentley and Merrill, which is incorporated by reference in Bentley, expressly disclose why the dendritic molecules of Bentley are useful. Ex. 1015, 3:10–16, 7:12–22; Ex. 2020, Abstract. This is sufficient to demonstrate a reasonable likelihood that claim 1 would have been obvious over Bentley.

Patent Owner also asserts that Petitioner has failed to demonstrate a reasonable expectation of success in increasing the molecular weight of Bentley's dendritic polymers to at least about 5,000 Da and still retain the desired activity of the target molecule. Prelim. Resp. 34–35. This argument is not persuasive for at least two reasons. First, Bentley is presumptively enabled and expressly discloses variable ranges for the dendritic polymer that result in a molecular weight above "at least about 5,000 Da." Ex. 1015, 7:12–22; *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1355 (Fed. Cir. 2003) (holding that issued patents are presumed enabled).

[redacted]

Second, there is ample evidence of record at this stage of the proceeding to support Petitioner's argument that one of ordinary skill in the art could successfully manipulate the length of PEG polymer arms to achieve a desired molecular weight for the entire PEG molecule. Ex. 1083 ¶¶ 245–283, 308,

On this record, Petitioner has demonstrated sufficiently that Bentley teaches or suggests every limitation of claim 1. Accordingly, Petitioner has demonstrated a reasonable likelihood that the subject matter of claim 1 of the '440 patent would have been obvious over the disclosures of Bentley. Pet. 18 (citing Ex. 1083 ¶¶ 305–06); *see E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018) (holding that an overlap in ranges "creates a presumption of obviousness").

3. Analysis of Claims 2–16, 19, 29, 30, and 32–35

Petitioner identifies where it contends Bentley teaches or suggests the subject matter of claims 2–16, 19, 29, 30, and 32–35. Pet. 20–31. Patent Owner does not specifically address these claims.

On this record, and upon review of Petitioner's arguments and evidence, we determine that Petitioner has demonstrated a reasonable likelihood that the subject matter of claims 2–16, 19, 29, 30, 32–35 would have been obvious over the disclosures of Bentley.

4. Analysis of Claims 20 and 31

Claims 20 and 31 each require a "biologically active conjugate." Ex. 1001, 25:27, 26:54. Petitioner contends one of ordinary skill in the art would have found it obvious to form a biologically active conjugate using the reactive aldehyde hydrate moiety of Bentley. Pet. 26, 30–31.

[redacted]

As noted by Patent Owner, the specific PEG compound relied upon by Petitioner is described in Bentley as a dendritic "star" molecule. Ex. 1015, 6:66–7:20; Prelim. Resp. 28–29. On this record, Petitioner does not explain sufficiently why one of ordinary skill in the art would have sought to conjugate a biologically active molecule to the aldehyde hydrate moiety of this PEG compound, which Merrill explains is useful for "separating and purifying therapeutic proteins." Ex. 1015, 5–8; Ex. 2020, Abstract. Accordingly, Petitioner has not demonstrated a reasonable likelihood of prevailing with respect to claims 20 and 31 over Bentley.

E. Obviousness of Claims 16–18 and 30 over Bentley and Liebigs

Claim 16 depends from claim 1 and further requires that "p is 0 and Y is a hydroxyl," claim 17 depends from claim 1 and further requires that "Y has the structure –O-Gp, wherein Gp is a protective group," and claim 18 depends from claim 17 and further requires that "Gp is selected from the group consisting of benzyl, acetal and dihydropyranyl." Ex. 1001, 25:10–16. Petitioner contends the subject matter of claims 16–18 and 30 would have been obvious over the combined disclosures of Bentley and Liebigs. Pet. 31–35.

Petitioner contends one of ordinary skill in the art would have understood that Bentley's dendritic molecule is formed using a "starting PEG" polymer and would have looked to Liebigs to determine how to best form this molecule. *Id*. at 32–34.

Patent Owner contends Petitioner's arguments fail because Liebigs is "not expressly directed to preparing branched polymers for use in conjugation of biologically active molecules" and because Petitioner has not explained sufficiently why one of ordinary skill in the art would have looked

[redacted]

specifically to the disclosures of Liebigs. Prelim. Resp. 36 (citing IPR2019-01392, Paper 1, 44).

On this record, Petitioner provides an explanation supported by record evidence as to why one of ordinary skill in the art seeking to form the dendritic "star" molecule of Bentley would have arrived at the limitations of claims 16–18 and 30. Although Patent Owner's arguments with respect to the combination of Bentley and Liebigs may have some merit, this factual issue is best resolved upon a full trial record.

In view of the foregoing, Petitioner has demonstrated a reasonable likelihood that claims 16–18 and 30 would have been obvious over Bentley and Liebigs.

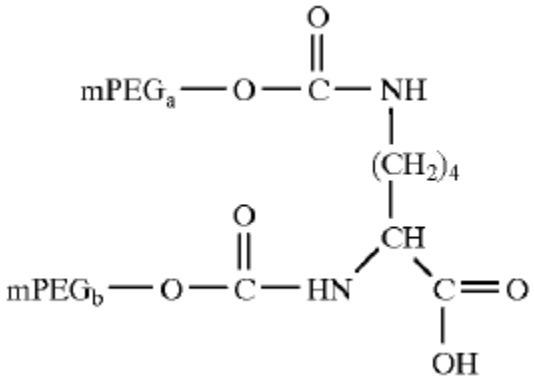
F. Obviousness of Claims 1–3, 5, 7–10, 12–16, 20, and 29–35 over Harris

Petitioner contends the subject matter of claims 1–3, 5, 7–10, 12–16, 20, and 29–35 would have been obvious over the disclosures of Harris. Pet. 39–53.

1. Harris

Harris discloses "[m]ulti-armed, monofunctional, and hydrolytically stable polymers" having two polymer arms. Ex. 1016, Abstract. A functional group on the polymer is used to link the polymer to a drug or biocatalyst. *Id*. at 1:36–40.

One example of the PEG molecules of Harris is reproduced below:



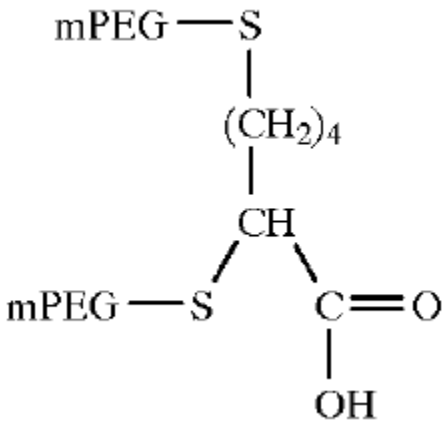
The figure above depicts one embodiment of Harris. *Id*. at 9:45–55. The polymer derivative is based upon the "hydrolytically stable coupling of mPEG to lysine." *Id*. at 9:35–38. The mPEG arms consist of CH_3O–$(CH_2CH_2O)_nCH_2CH_2$– and provide molecular weights "of from about 100 to 100,000." *Id*. at 9:35–55. The reactive carboxyl moiety of this molecule provides a linkage to reactive sites on proteins, enzymes, nucleotides, lipids, liposomes, and other materials. *Id*. at 9:20–22, 9:42–43.

Harris explains that the mPEG disubstituted lysine of the invention may be made using a one-step method or a two-step method. *Id*. at 11:46–58, 18:15–22. The mPEG disubstituted lysine made by the one-step method typically has a molecular weight of 40,000 and the mPEG disubstituted lysine made by the two-step method typically has a molecular weight of 10,000. *Id*. at 18:11–22. Harris notes, however, that mPEG disubstituted lysines may have molecular weights as high as about 100,000 and as low as about 100 to 200. *Id*. at 18:31–45.

Harris discloses that a wide variety of hydrolytically stable linkages may be used, "although not necessarily with equivalent results." *Id*. at 18:46–48, 18:56–58. These linkages may include the carbamate linkage shown in the figure above, or other linkages such as amine or thioether

[redacted]

linkages. *Id*. at 18:58–62, 19:12–23:20. An mPEG disubstituted lysine using a thioether linkage is reproduced below:



As shown in the figure above, the mPEG disubstituted lysine contains two mPEG arms attached using thioether linkages as well as a reactive carboxyl moiety. *Id*. at 9:56–60, 12:10–16, 23:11–20.

2. Analysis of Claim 1

Petitioner contends the mPEG disubstituted lysine described above expressly discloses every limitation of claim 1, except a molecular weight of "at least about 5,000." Pet. 40. Petitioner further contends, however, that one of ordinary skill in the art would have formed this molecule with a molecular weight of 10,000 Da or 40,000 Da based on Harris's express disclosures of achieving these molecular weights using the one- or two-step methods. *Id*. at 40–41. Petitioner further notes that Harris discloses a 10,000 Da carbamate-linked polymer conjugated to asparaginase that provided an increase in blood circulation half-life from 27 minutes to 2,600 minutes. *Id*. at 41 (citing Ex. 1016, 30:66–31:27, 31:65–32:40, 35:40–57). According to Petitioner, "[b]ecause Harris['s] heteroatom polymers are described as hydrolytically stable alternatives to the carbamate-linked polymer used [in the comparative tests], a [person of ordinary skill in the art]

would expect similar properties would be achieved" using the mPEG disubstituted lysines described above. *Id*.

Patent Owner contends Petitioner's arguments fail because it has not demonstrated that the –COOH moiety of Harris is a "functional group." Prelim. Resp. 38–39.

With respect to the term "functional group," the '440 patent explains that

> the terms 'functional group,' 'active moiety,' 'reactive site,' 'chemically reactive group,' and 'chemically reactive moiety' are used in the art and herein to refer to distinct, definable portions or units of a molecule. The terms are somewhat synonymous in the chemical arts and are used here to indicate the portions of molecules that perform some function or activity and are reactive with other molecules.

Ex. 1001, 3:35–42.

Dr. Yamamoto testifies that one of ordinary skill in the art would understand that both the carboxyl and hydroxyl groups of Harris represent a "functional group" that is "reactive with an electrophilic or nucleophilic group." Ex. 1083 ¶¶ 381, 384–85; Pet. 38–39. This testimony is generally consistent with the '440 patent's explanation that a "functional group" is a "distinct, definable" portion of a molecule that performs some function or activity and is reactive with other molecules. Ex. 1001, 3:35–42.

As Patent Owner notes, Harris describes the –COOH moiety as a "reactive site" that can be "converted to a functional group for selective reactions." Prelim. Resp. 38–39 (citing Ex. 1016, 12:10–12). The question, however, is not what Harris considers a "functional group," but what one of ordinary skill in the art would consider a "functional group" upon reading the intrinsic record of the '440 patent. And on this record, Dr. Yamamoto's

[redacted]

testimony that the —COOH molecule of Harris would be considered a "functional group" is both unrebutted and consistent with the use of that term in the '440 patent.[13] Ex. 1083 ¶¶ 381, 384–85. Thus, Petitioner has demonstrated sufficiently for purposes of institution that the –COOH group of Harris is a "functional group."

Patent Owner also contends that Petitioner has failed to explain sufficiently why one of ordinary skill in the art would have selected the amine- and thioether-linked polymers of Harris for further development. Prelim. Resp. 40. We are not persuaded by this argument. Harris discloses inventive mPEG disubstituted lysines having a molecular weight of 10,000 or 40,000 Da that are useful for conjugation to proteins. Ex. 1016, 7:50–54, 18:15–22. Harris also discloses that conjugation of an mPEG disubstituted lysine with a molecular weight of 10,000 Da to asparaginase resulted in an improvement of blood clearance half-life from 27 minutes to 2,600 minutes. *Id*. at 30:65–31:2, 35:40–57. On this record, Petitioner sufficiently explains why these disclosures would have taught or suggested using amine- and thioether-linked disubstituted lysines with a molecular weight of either 10,000 or 40,000 Da.

As Patent Owner notes, the disubstituted lysine utilized in Harris's comparative testing had a different linker (carbamate-linked) than the disubstituted lysines relied upon by Petitioner (amine-linked and thioether-

[13] The identified disclosures of Harris indicate that –COOH may be "converted to a functional group *for selective reactions*." Ex. 1016, 12:10–13 (emphasis added). Patent Owner does not explain why this disclosure suggests that –COOH is not a functional group, as opposed to indicating that –COOH is a functional group that is not yet selective for certain intended reactions.

linked). Prelim. Resp. 38, 43–44. Petitioner provides a sufficient explanation at this stage of the proceeding, however, to explain why one of ordinary skill in the art would have expected similar results using any of the identified carbamate-, thioether-, and amine-linked polymers of Harris. Pet. 41 (citing Ex. 1083 ¶ 387).

Patent Owner also argues that Petitioner has failed to demonstrate a reasonable expectation of success in modifying the PEG compounds of Harris to have a molecular weight of at least about 5,000 Daltons. Prelim. Resp. 41–42. We are not persuaded by this argument because Harris specifically discloses that molecular weights of 10,000 and 40,000 may be used and provides specific methods for forming such compounds. Ex. 1016, 18:4–7, 18:23–45; Pet. 40–41.

Patent Owner also argues that there would have been no reasonable expectation of success in forming the disubstituted lysines of Harris in view of the '440 patent's disclosure that Harris's methods of forming branched PEG molecules require difficult and extensive purification processes prior to attachment of the PEG polymers to the core molecule. Prelim. Resp. 45 (citing Ex. 1001, 1:55–2:3). This argument is not persuasive because the '440 patent expressly indicates that the PEG polymers of Harris may be successfully prepared and used, and a reasonable expectation of success does not require evidence that success would be achieved in an easy or inexpensive manner.

In view of the foregoing, we determine that Petitioner has demonstrated a reasonable likelihood that claim 1 of the '440 patent would have been obvious over Harris.

[redacted]

3. Analysis of Claims 2, 3, 5, 7–10, 12–16, 20, and 29–35

Petitioner provides analysis and citations to record evidence to show where Harris teaches or suggests every limitation of claims 2, 3, 5, 7–10, 12–16, 20, and 29–35. Pet. 42–52. Patent Owner does not specifically address Petitioner's arguments or cited evidence.

On the record, Petitioner has demonstrated sufficiently that Harris teaches or suggests every limitation of claims 2, 3, 5, 7–10, 12–16, 20, and 29–35. Thus, we determine that Petitioner has demonstrated a reasonable likelihood that the subject matter of claims 2, 3, 5, 7–10, 12–16, 20, and 29–35 would have been obvious over Harris.

G. Anticipation of Claims 29 and 31 by Harris

Claims 29 and 31 do not contain a limitation on the molecular weight of the polymer molecule. Petitioner contends these claims are anticipated by Harris. Pet. 53–55.

Patent Owner contends claims 29 and 31 are not anticipated by Harris because Petitioner has not demonstrated that the –COOH group of Harris is a "functional group." Prelim. Resp. 45–46.

For the reasons discussed above in Section II.F.2, Petitioner has set forth sufficient argument and evidence for purposes of institution to show that the –COOH group of Harris is a "functional group." Pet. 53–54 (citing Ex. 1083 ¶ 428); *see* Ex. 1083 ¶¶ 381, 384). Thus, Petitioner has demonstrated a reasonable likelihood that claims 29 and 31 of the '440 patent are anticipated by Harris.

H. Anticipation of Claims 1–15, 17, 19, 20, 29, 31–33, and 35 by JP-542

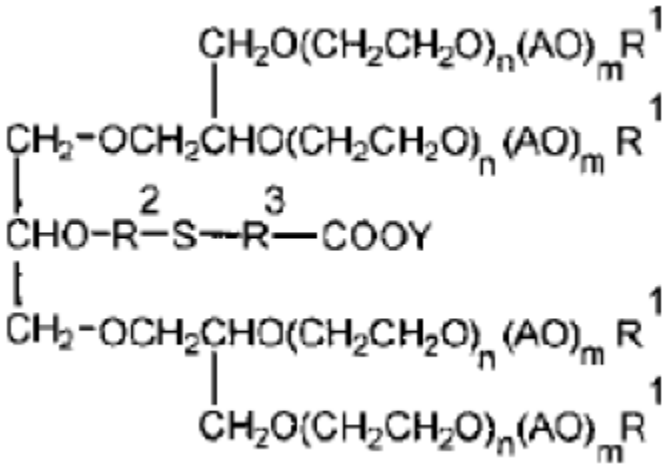
Petitioner contends claims 1–15, 17, 19, 20, 29, 31–33, and 35 are anticipated by JP-542. Pet. 56–75.

[redacted]

1. JP-542

JP-542 discloses "a carboxyl-group-containing polyoxyalkylene compound that is used to modify a compound or a drug" in order to stabilize the drug, decrease its antigenicity, or prolong its residence time in the blood. Ex. 1017, Abstract.

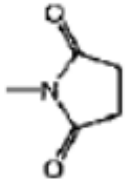
Formula (1) of JP-542 is reproduced below:



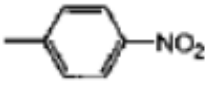
(1)

Formula (1) illustrates the general structure of the inventive polyoxyalkylene compounds of JP-542. *Id.* ¶ 6. In formula (1), R1 is a hydrogen atom, a 1 to 24 carbon hydrocarbon, or a 1 to 24 carbon acyl group; R2 is a 3 or 4 carbon hydrocarbon; R3 is a 1 to 10 carbon hydrocarbon; AO is a 3 or 4 carbon oxyalkylene; Y is either a hydrogen atom or an active group illustrated by formula (2) or (3); n is 1 to 1000; m is 0 to 250; and n/(n+m) is no less than 0.8; wherein the oxyethylene and the 3 or 4 carbon oxyalkylene "may be added in blocks or randomly." *Id.* ¶ 8.

Formulas (2) and (3) of JP-542 are reproduced below:



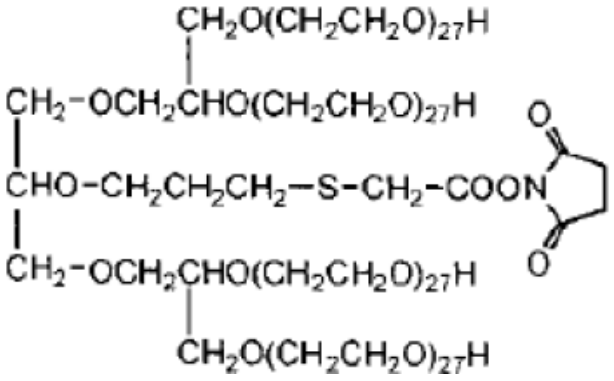
(2)



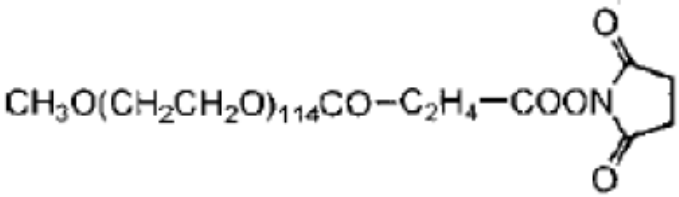
(3)

Formulas (2) and (3) represent preferred active groups for use in the compound of formula (1). *Id*. ¶17.

JP-542 also discloses example compound species falling within the scope of formula (1) that may be conjugated with a compound or drug. The compounds of formulas (14) and (15) are reproduced below:



(14)



(15)

Formula (14) depicts a branched polyalkylene compound and formula (15) depicts a linear polyalkylene compound, both of which are conjugated to the active group illustrated in formula (2). *Id*. ¶¶ 9, 52, 56.

In Test Example 1 of JP-542 the compound of formula (14) was reacted with L-asparaginase and in Comparative Test Example 1 the linear compound of Formula (15) was reacted with L-asparaginase. *Id*. ¶¶ 54–57. The resulting PEGlyated compounds were then tested for antigenicity and enzyme activity. *Id*. ¶¶ 57–58, Table 1. The results from these tests are reproduced below:

Table 1

	PEG derivative (Mw)	No. of bound amino groups[a)]	Enzyme activity		Antibody binding capacity
			Method A	Method B	
Test example 1	5, 162	50	35	40	0
Comparative test example 1	5, 200	54	15	22	35

a) Number of amino groups bound to the compound among amino groups in asparaginase molecule (ninety-two)

Table 1 provides the test results for Test Example 1 and Comparative Test Example 1. As shown in Table 1, the compound of Test Example 1 had zero antigenicity yet still retained 35 to 40 % of its enzyme activity. *Id*. ¶¶ 54, 58. Conversely, the compound of Comparative Test Example 1 had an antibody binding capacity of 35% (i.e., some level of antigenicity) and retained only 15 to 22% of its enzyme activity. *Id*. ¶¶ 54–58.

2. Analysis of Claims 1–15, 17, 19, 20, 32, 33, and 35

Claims 1–15, 17, 19, 20, 32, 33, and 35 each require that the branched reactive polymer has a molecular weight of "at least about 5,000 Da." Petitioner contends the polymer of formula (14) of JP-542 has a reported molecular weight of 5,162 and the polymer of formula (8) has a reported molecular weight of 4,965 Da, which Petitioner asserts is "at least about 5,000 Da." Pet. 58–59 (citing Ex. 1017 ¶ 58).

For purposes of the '440 patent, molecular weight is calculated by summing the weight of all polymer molecules. Ex. 1001, 4:51–63. The capping groups, linker molecules, and heteroatoms present in these molecules are not included. *Id*. Consistent with this approach, Petitioner does not include non-polymer molecules in its calculation of molecular weight for its ground based on Bentley. Pet. 18 n.6.

On this record, we agree with Patent Owner that Petitioner has not demonstrated that the branched PEG compounds of JP-542 have a molecular weight of "at least about 5,000 Da" when the calculation methodology of the '440 patent is utilized. Prelim Resp. 47–50. Conversely, Patent Owner provides calculations demonstrating that the compounds of formulas (8) and (14) of JP-542 have a molecular weight of 4,752 using the calculation methodology of the '440 patent. *Id*. at 49–50. Accordingly, on this record, Petitioner has not demonstrated a reasonable likelihood that claims 1–15, 17, 19, 20, 32, 33, and 35 are anticipated by JP-542.

3. Analysis of Claims 29 and 31

Claims 29 and 31 of the '440 patent do not require a particular molecular weight for the branched reactive polymer. Ex. 1001, 26:14–35, 26:54–27:9. On this record, Petitioner sufficiently demonstrates that the branched polymers of formula (10) and formula (12) of JP-542 disclose each limitation of claim 29 and that the branched polymer of Test Example 1 discloses each limitation of claim 31. Pet. 70–75. Patent Owner does not offer, at this stage, any arguments addressing Petitioner's showing for these claims, beyond the arguments addressed above for independent claim 1. *See generally* Prelim. Resp. 47–50. Accordingly, Petitioner has demonstrated a

reasonable likelihood that claims 29 and 31 of the '440 patent are anticipated by JP-542.

I. Obviousness of Claims 1–15, 17, 19, 20, 29, and 31–35 over JP-542 and MDD

Petitioner contends the subject matter of claims 1–15, 17, 19, 20, 29, and 31–35 would have been obvious over the combined disclosures of JP-542 and MDD. Pet. 75–78.

1. MDD

MDD "traces the development of PEGASYS, a polyethylene glycol (PEG)-modified IFN-α-2a designed to improve upon the pharmacokinetics of IFN-α therapy." Ex. 1029, 1. The branched PEG moiety of MDD consists of two monomethoxy PEG chains, each with an average molecular weight of 20,000 Da. *Id*. at 4. "The two monomethoxy PEG chains are branched together through a lysine molecule via urethane bonds, one at the α-amino group and the other at the ε–amino group of the lysine linker." *Id*.

It was determined that that 40 kDa branched mono-PEG-IFN-α-2a had an optimal pharmacological profile and superior efficacy compared to IFN-α-2a monotherapy. *Id*. at 4–5.

2. Analysis

Petitioner contends a person of ordinary skill in the art would have found it obvious to prepare branched polymers by the process of JP-542 and optimize the molecular weight of such polymers through routine experimentation for each selected biologically active molecule, as taught by MDD. Pet. 76. Petitioner further contends one of ordinary skill in the art would have found it obvious to prepare the JP-542 polymers of formula (14) with a total molecular weight of 40 kDa for conjugation to IFN-α-2a, as taught by MDD. *Id*.

[redacted]

Petitioner does not actually compare the chemical structures of the conjugates disclosed in JP-542 and MDD, or persuasively explain why one of ordinary skill in the art would have sought to modify the successful PEGASYS product of MDD by substituting its PEG backbone with the PEG of formula (14). *See generally* Prelim. Resp. 50–53. Nor does Petitioner sufficiently explain why one of ordinary skill in the art seeking to conjugate a compound other than asparaginase to a PEG compound would have selected formula (14) for this purpose. Accordingly, based on the current record, we are not persuaded that Petitioner has demonstrated a reasonable likelihood that claims 1–15, 17, 19, 20, 29, and 31–35 would have been obvious over JP-542 and MDD.

J. Obviousness of Claims 16–18 and 30 over JP-542 and Bentley

Petitioner contends the subject matter of claims 16–18 and 30 would have been obvious over the combined disclosures of JP-542 and Bentley. Pet. 78–80.

Petitioner asserts that it "would have been obvious to a [person of ordinary skill in the art] to deprotect the JP-542 allyl protected hydroxyl (formula (8) in order to activate the JP-542 polymer as an aldehyde hydrate as taught by Bentley." *Id*. at 79 (Ex. 1083 ¶¶ 486–87). According to Petitioner, "JP-542 and Bentley would have been a natural combination since both concern branched poly(alkene glycol) polymers." *Id*.

The compound of formula (8) does not fall within the broad genus of the inventive formula of JP-542 (i.e., formula (1)) and appears to be a precursor molecule used to manufacture other PEG polymers discussed in the reference. Ex. 1017, 4 (noting that the "present invention" of JP-542 is illustrated in formula (1)), 11 (using the compound of formula (8) to

[redacted]

manufacture the compound of formula (11), which is in turn used to create the compound of formula (14)). We agree with Patent Owner that Petitioner has not explained sufficiently why one of ordinary skill in the art would have sought to modify such a precursor compound with an aldehyde hydrate moiety. *See generally* Prelim. Resp. 53–55. Accordingly, on this record, we are not persuaded that Petitioner has demonstrated a reasonable likelihood that the subject matter of claims 16–18 and 30 would have been obvious over JP-542 and Bentley.

K. 325(d)

Harris was entered into the prosecution of the '440 patent in at least three ways. Prelim. Resp. 58. First, Harris is discussed in the Specification of the '440 patent. Ex. 1001, 1:55–2:3. Second, Harris was submitted on an IDS. Ex. 1008, 84. Third, Harris was identified in a third party submission provided during prosecution. Prelim. Resp. 58 (citing Ex. 1001, 1:55–2:3; Ex. 2001, 60, 159–161, 613). Because Harris was before the Examiner during prosecution, Patent Owner contends we should exercise our discretion to deny the Petition under 35 U.S.C. § 325(d), at least with respect to the grounds based on Harris. *Id*. at 60.

Having determined that the remaining asserted grounds support institution of all the challenged claims, we will institute on all grounds presented in the Petition.[14] *See SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1353 (2018); *see also PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (interpreting the statute to require "a simple yes-or-no

[14] Although Harris was identified during prosecution, we are presented with no evidence that the Examiner utilized Harris in a ground of rejection or that the Examiner analyzed the same portions of Harris that are relied upon in the Petition.

[redacted]

institution choice respecting a petition, embracing all challenges included in the petition"). Thus, we decline to exercise our discretion under 35 U.S.C. § 325(d).

L. 314(a)

Patent Owner requests that the Board deny the Petition due to a parallel district court proceeding that will resolve at least ten months before a final written decision is due to issue in this proceeding. Prelim. Resp. 60–61 (citing Ex. 2021). Patent Owner concedes, however, that the '440 patent is no longer asserted in the district court proceeding. *Id*. at 61. Thus, the district court will not be presented with, and will not decide, the same issues presented in this proceeding. Accordingly, we decline to exercise our discretion under 35 U.S.C. § 314(a).

M. Arthrex

Patent Owner argues that "[b]ecause Administrative Patent Judges ('APJs'), who preside over proceedings before the Board, are not appointed by the President and confirmed by the Senate, they are not empowered to institute *inter partes* review or render a final written decision . . . ." Prelim. Resp. 63. Patent Owner further argues that, notwithstanding the Federal Circuit's recent opinion in *Arthrex v. Smith & Nephew*, No. 18-2140, slip. op. at 25–29, (Fed. Cir. Oct. 31, 2019), 'the statutory limitations on the removal of APJs' under Title 5 are not severable by the Federal Circuit." *Id*. at 64. Thus, according to Patent Owner, "any institution or final written decision" in this case is "invalid." *Id*.

Patent Owner's arguments do not support denial of institution because, *inter alia*, this case is at the institution stage and *Arthrex* indicates that there is "no constitutional infirmity" with respect to an institution

[redacted]

decision. *Arthrex, Inc. v. Smith & Nephew, Inc.*, 941 F.3d 1320, 1340 (Fed. Cir. 2019) (determining that the statute "clearly bestows such authority on the Director pursuant to 35 U.S.C. § 314").

CONCLUSION

In view of the foregoing, and for the reasons discussed above, Petitioner has demonstrated a reasonable likelihood of prevailing with respect to at least one claim of the '440 patent. Thus, we institute an *inter partes* review with respect to all challenged claims and on all asserted grounds set forth in the Petition.

ORDER

In view of the foregoing, it is:

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted on all challenged claims of the '440 patent and on all asserted grounds set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(a) and 37 C.F.R. § 42.4, notice is hereby given of the institution of trial, which shall commence on the entry date of this decision.

[redacted]

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