UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC., and CELLTRION, INC.,

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,

Patent Owner.

IPR2022-01225[1]
U.S. Patent No. 10,130,681

PATENT OWNER'S NOTICE OF APPEAL

[1] IPR2023-00532 has been joined with this proceeding.

By Electronic Filing
Patent Trial and Appeal Board
U.S. Patent & Trademark Office
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U.S. Patent & Trademark Office
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Alexandria, VA 22314-5793

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Circuit Executive and Clerk of Court
United States Court of Appeals for the Federal Circuit
717 Madison Place, NW
Washington, DC 20439

Pursuant to 35 U.S.C. §§ 141(c), 142, and 319, and 37 C.F.R. § 90.2(a) and 90.3(a), notice is hereby given that Patent Owner Regeneron Pharmaceuticals, Inc. ("Patent Owner") appeals to the United States Court of Appeals for the Federal Circuit from the Final Written Decision entered January 9, 2024 (Paper 96) in IPR2022-01225, attached as Exhibit A, and all prior and interlocutory rulings related thereto or subsumed therein.

In accordance with 37 C.F.R. § 90.2(a)(3)(ii), Patent Owner indicates that the issues for appeal include the holding that claims 1, 3-11, 13, 14, 16-24, and 26 of United States Patent No. 10,130,681 (the "'681 Patent") were shown unpatentable; and any finding or determination supporting or related to these

issues, and all other issues decided adversely to Patent Owner in any orders, decisions, rulings, and opinions underling or supporting the Final Written Decision, including, without limitation, the Board's construction and application of the claim language, the Board's interpretation of the prior art, the Board's interpretation of expert evidence, and the Board's application of the law. Among the issues for appeal are (1) the Board's construction of "method for treating"; (2) the Board's application of the printed matter doctrine; (3) the Board's determination that claims 1, 3-11, 13, 14, 16-24, and 26 of the '681 Patent are inherently anticipated by Dixon; (4) the Board's incorporation by reference of flawed reasoning from an earlier decision and (5) the Board's decision denying-in-part and dismissing-in-part PO's motion to exclude.

Pursuant to 37 C.F.R. § 90.3, this Notice of Appeal is timely, having been duly filed within 63 days after the date of the Final Written Decision.

A copy of this Notice of Appeal is being filed simultaneously with the Patent Trial and Appeal Board, the Clerk's Office for the United States Court of Appeals for the Federal Circuit, and the Director of the U.S. Patent and Trademark Office.

Dated: March 12, 2024

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned certifies that the original of this **PATENT OWNER'S NOTICE OF APPEAL** was filed via hand delivery on March 12, 2024 with the Director of the United States Patent and Trademark Office at the address below:

Office of the General Counsel
U.S. Patent & Trademark Office
Madison Building East, 10B20
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Alexandria, Virginia 22314-5793

A copy of this Notice of Appeal is being filed and served on March 12, 2024 as follows:

USPTO Patent Trial and Appeal Board:
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(via email pursuant to 37 C.F.R. § 42.6(e))

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Exhibit A

Trials@uspto.gov
571-272-7822

Paper 96
Date: January 9, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,

Patent Owner.

IPR2022-01225[1]
Patent 10,130,681 B2

Before JOHN G. NEW, SUSAN L. C. MITCHELL, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

NEW, Administrative Patent Judge.

JUDGMENT
Final Written Decision
Denying in Part, Granting in Part, and Dismissing in Part Petitioner's Motion to Exclude Evidence, Denying in Part and Dismissing in Part Patent Owner's Motion to Exclude Evidence, Determining Challenged Claims 1, 3–11, 13, 14, 16–24, and 26 Unpatentable
35 U.S.C. § 318(a)

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[1] IPR2023-00532, *Celltrion, Inc. v. Regeneron Pharms. Inc.*, has been joined with this proceeding. *See* Paper 38.

I. INTRODUCTION

We have jurisdiction to hear this *inter partes* review under 35 U.S.C. § 6. This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons set forth below, we determine that Petitioner Mylan Pharmaceuticals Inc. ("Petitioner") has established, by a preponderance of the evidence, that challenged claims 1, 3–11, 13, 14, 16–24, and 26 of Patent Owner Regeneron Pharmaceuticals, Inc.'s ("Patent Owner") U.S. Patent No. 10,130,681 B2 (Ex. 1001, the "'681 patent") are unpatentable. We also grant in part, deny in part, and dismiss in part Petitioner's Motion to Exclude Evidence and deny in part and dismiss in part Patent Owner's Motion to Exclude Evidence.

A. Procedural History

On July 1, 2022, Petitioner filed its Petition (Paper 2, "Petition") seeking *inter partes* review of claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent. Patent Owner timely filed a Preliminary Response. Paper 14 ("Prelim. Resp."). With our authorization, Petitioner filed a Preliminary Reply and Patent Owner filed a Preliminary Sur-Reply. Paper 16 ("Prelim. Reply"); Paper 18 ("Prelim. Sur-Reply"). On January 1, 2022, and pursuant to 35 U.S.C. § 314, we instituted *inter partes* review of challenged claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent. Paper 21 ("Institution Decision" or "Dec.").

After institution of trial, Patent Owner filed a Response (Paper 41[2], "PO Resp."), to which Petitioner filed a Reply (Paper 60, "Pet. Reply"), and Patent Owner, in turn, filed a Sur-Reply (Paper 65, "Sur-Reply").

Both Petitioner (Paper 76) and Patent Owner (Paper 77) filed Motions to Exclude Evidence ("Mot. Exclude") and filed Oppositions (Papers 82 and 80, respectively) to the opposing party's Motion to Exclude Evidence (Opp. Mot. Exclude). Both parties also filed a Reply to their opponent's Opposition to their Motions to Exclude ("Reply Mot. Exclude"). Paper 83 (Petitioner), Paper 84 (Patent Owner).

II. BACKGROUND

A. Real Parties-in-Interest

Petitioner identifies Viatris Inc., Mylan Inc., Mylan Pharmaceuticals Inc., Momenta Pharmaceuticals, Inc., Janssen Research & Development LLC, Johnson & Johnson, Biocon Biologics Inc., Biocon Limited, Biocon Biologics Limited, Biocon Biologics UK Limited, and Biosimilar Collaborations Ireland Limited as real parties-in-interest. Paper 56 at 1. Patent Owner identifies Regeneron Pharmaceuticals, Inc. as the real party-in-interest. Paper 72 at 2.

B. Related Matters

Petitioner and Patent Owner identify *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-00880, IPR2021-00881, IPR2022-01226

[2] Papers 41, 60, and 76 of the record are the unredacted versions of these papers. Papers 42, 59, 75 are the redacted versions.

(PTAB), and *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.) as related matters. Paper 5, 1; Paper 6, 1. Patent Owner also identifies *Chengdu Kanghong Biotechnology Co. v. Regeneron Pharms., Inc.*, PGR2021-00035 (PTAB) (proceeding terminated before institution). Paper 5, 2–3. Petitioner further identifies the following as judicial or administrative matters that would affect, or be affected by, a decision in this proceeding: *Apotex Inc. v. Regeneron Pharmaceuticals, Inc.*, No. IPR2022-01524 (PTAB), *United States v. Regeneron Pharms., Inc.*, No. 1:20-cv-11217-FDS (D. Mass.), and *Horizon Healthcare Servs., Inc. v. Regeneron Pharms., Inc.*, No. 1:22-cv-10493-FDS (D. Mass.). Paper 6, 1–2.

Petitioner also identifies additional patents and patent applications that claim priority to the '681 patent, namely: US 9,254,338 B2; US 9,669,069 B2; US 10,857,205 B2; US 10,828,345 B2; US 10,888,601 B2; US 11,253,572 B2; and US Appl. Ser. Nos. 17/072,417; 17/112,063; 17/112,404; 17/350,958; and 17/740,744. Paper 6, 2.

On March 22, 2023, this *inter partes* review was joined with IPR2023-00532, *Celltrion, Inc. v. Regeneron Pharms. Inc.* (the "'532 IPR"), which also challenged claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent. *See* Paper 38. Petitioner Celltrion Inc. acted as a "silent understudy" in the present proceeding, and a copy of this Final Written Decision will be entered in the '532 IPR.

Of particular relevance to our decision in this proceeding is the Final Written Decision entered in IPR2021-00881 (the "-00881 IPR") on November 9, 2022. *See* IPR 2021-00881, Paper 94 (the "-00881 Decision," Ex. 3001). Both the '681 patent and US 9,254,338 B2 (the "'338 patent") at issue in IPR2021-00881 share a common Specification. *See generally*,

Ex. 1001; IPR2021-00881, Ex. 1001. In the -00881 Decision, the panel found that the challenged claims were unpatentable on at least one of the same grounds asserted against the challenged claims in the present Petition. *See generally* Ex. 3001.

C. The Asserted Grounds of Unpatentability

Petitioner contends that claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent are unpatentable, based upon the following grounds:

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1	1, 3–11, 13, 14, 16–24, 26	102[3]	Dixon[4]
1	1, 3–11, 13, 14, 16–24, 26	102	Adis[5]

[3] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, 125 Stat. 284 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the application from which the '681 patent issued has an effective filing date after that date, the AIA versions of §§ 102 and 103 apply.

[4] J.A. Dixon et al., *VEGF Trap-Eye for the Treatment of Neovascular Age-Related Macular Degeneration*, 18(10) EXPERT OPIN. INVESTIG. DRUGS 1573–80(2009) ("Dixon") Ex. 1006.

[5] Adis R&D Profile, Aflibercept: AVE 0005, AVE 005, AVE0005, VEGF Trap – Regeneron, VEGF Trap (R1R2), VEGF Trap-Eye, 9(4) DRUGS R D 261–269 (2008) ("Adis") Ex. 2007.

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
3	1, 3–11, 13, 14, 16–24, 26	102	Regeneron 2008[6]
4	1, 3–11, 13, 14, 16–24, 26	103	Dixon alone or in view of Papadopoulos[7] and/or Wiegand[8]
5	1, 3–11, 13, 14, 16–24, 26	103	Dixon in combination with Rosenfeld[9], and if necessary, Papadopoulos patent and/or Wiegand
6	1, 3–11, 13, 14, 16–24, 26	103	Dixon in combination with Heimann-2007, and if necessary, Papadopoulos and/or Wiegand

Petitioner also relies upon the Declarations of Dr. Thomas A. Albini (the "Albini Declaration," Ex. 1002) and Dr. Mary Gerritsen (the "Gerritsen Declaration," Ex. 1003). Patent Owner relies upon the Declarations of

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[6] Press Release, Regeneron and Bayer HealthCare Announce Encouraging 32-Week Follow-Up Results from a Phase 2 Study of VEGF Trap-Eye in Age-Related Macular Degeneration (April 28, 2008) ("Regeneron 2008") Ex. 1012.

[7] Papadopoulos et al. (US 7,374,758 B2, May 20, 2008) ("Papadopoulos") Ex. 1010.

[8] Wiegand et al. (US 7,531,173 B2, May 12, 2009) ("Wiegand") Ex. 1007.

[9] P.J. Rosenfeld et al., *Ranibizumab for Neovascular Age-Related Macular Degeneration*, 355 (14) N. ENGL. J. MED. 1419–31; Suppl. App'x 1–17 (2006) ("Rosenfeld") Ex. 1058.

Dr. Diana V. Do (the "Do Declaration," Ex. 2056), Dr. Alexander M. Klibanov (the "Klibanov Declaration," Ex. 2057), David M. Brown (the "Brown Declaration," Ex. 2055), and Dr. Richard Manning (the "Manning Declaration," Ex. 2059). We have reviewed the credentials of Petitioner's and Patent Owner's declarants, and consider each to be qualified to provide the opinions for which their testimony has been submitted.

D. The '681 Patent

The '681 patent is directed to methods for treating angiogenic eye disorders by sequentially administering multiple doses of a vascular epithelial growth factor ("VEGF") antagonist to a patient. Ex. 1001, Abstr. These methods include the administration of multiple doses of a VEGF antagonist to a patient at a frequency of once every 8 or more weeks, and are useful for the treatment of angiogenic eye disorders such as, *inter alia*, age related macular degeneration. *Id.*

In an exemplary embodiment, a single "initial dose" of VEGF antagonist ("VEGFT") is administered at the beginning of the treatment regimen (i.e., at "week 0"), two "secondary doses" are administered at weeks 4 and 8, respectively, and at least six "tertiary doses" are administered once every 8 weeks thereafter (i.e., at weeks 16, 24, 32, 40, 48, 56, etc.). Ex. 1001, col. 2, ll. 56–62.

E. Representative Claim

Claim 1 is representative of the challenged claims, and recites:

> 1. A method for treating an angiogenic eye disorder in a patient, said method comprising sequentially administering to the patient a single initial dose of a VEGF antagonist, followed

> by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;
>
> wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and
>
> wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
>
> wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130-231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232-457 of SEQ ID NO:2;
>
> wherein exclusion criteria for the patient include all of:
>
> (1) active intraocular inflammation;
>
> (2) active ocular or periocular infection;
>
> (3) any ocular or periocular infection within the last 2 weeks.

Ex. 1001, col. 21, ll. 40–63.[10]

F. Priority History of the '681 Patent

The '681 patent issued from U.S. Application Ser. No. 15/471,506 (the "'506 application") filed on March 28, 2017, and claims the priority

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[10] For the purposes of this Decision, the terms "aflibercept" and "VEGF Trap-Eye" are used to refer to the same active VEGF antagonist that is recited in challenged claim 1 as "a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130-231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232-457 of SEQ ID NO:2." *See, e.g.*, Ex. 1006, 1575 ("VEGF Trap-Eye and aflibercept … have the same molecular structure."

benefit of, *inter alia*, US Provisional Application Ser. No. 61/432,245, which was filed on Jan. 13, 2011. Ex. 1001, code (60).

The claims of the '681 patent, including challenged claims 1, 3–11, 13, 14, 16–24, and 26, were allowed on July 26, 2018, and the patent issued on November 20, 2018. Ex. 1017, 509; Ex. 1001, code (45).

III. MOTIONS TO EXCLUDE EVIDENCE

Both parties have submitted Motions to Exclude Evidence (Papers 76, 77) and have also filed Oppositions (Papers 82, 80) and Replies (Papers 83, 84) to the opposing party's Motion to Exclude. We now consider each party's Motion to Exclude in turn.

A. Petitioner's Motion to Exclude

Petitioner moves to exclude Patent Owner's Exhibits 2037–2039, 2079, 2080, 2084, 2085, 2098, 2101, 2103, 2104, 2122, 2136, 2138–40, 2163, 2169, 2170, 2176, 2190, 2197, 2200, 2208, 2218, 2229, 2243, 2244, 2250, 2259, 2277–79, 2282–85, 2298, 2299, and portions of Exhibits 2055–57 and 2059. Pet. Mot. Exclude, 1. We address each of Petitioner's arguments in turn.

1. Exhibits 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, 2282–85, and portions of Exhibit 2059 (¶¶ 11, 28, 29, 43, 47, 50–55, 60, 61, 63–69, 72, 74, 75, 78, 84, 108, 109, 113–16)

Petitioner argues that Patent Owner relies on the testimony of its expert, Dr. Manning, in support of its commercial success contentions. Pet. Mot. Exclude 1 (citing, e.g., PO Resp. 2, 49, 68–69; PO Sur-Reply, 25–28). Petitioner asserts that Dr. Manning in turn relies on various documents

purporting to reflect profit and loss statements for Patent Owner's product. *Id.* at 2 (citing Exs. 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, 2282–85, and Ex. 2059 at Attachments C1–C12, D1–D4, D7, and X2 (collectively, the "Financial Exhibits")). Petitioner also argues for exclusion of portions of Dr. Manning's Declaration relating to this evidence, i.e., Ex. 2059 ¶¶ 11, 28–29, 43, 47, 50–55, 60–61, 63–69, 72, 74–75, 78, 84, 108–09, 113–16. *Id.* Petitioner states that it timely objected to the challenged Financial Exhibits. *Id.* (citing Papers 23, 48).

Petitioner seeks exclusion of the Financial Exhibits on the bases of: (1) FRE 1006 (compilations of sales data created for this proceeding, without production of the underlying business records); (2) FRE 901 (lack of authentication by a witness with personal knowledge); (3) FRE 801–03 (hearsay of records not within the business record exception); and FRE 702 (alleged unreliability of expert testimony).

As Petitioner states, Patent Owner relies upon these Exhibits as objective secondary evidence of non-obviousness. *See, e.g.*, PO Resp. 65–69. However, and as we explain below, because we find that the challenged claims are anticipated by Dixon, we do not reach Patent Owner's arguments that the claims are non-obvious (Grounds 4–6) or its contentions regarding secondary considerations of non-obviousness. *See Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1364 (Fed. Cir. 2008) (holding that "secondary considerations are not an element of a claim of anticipation"). Consequently, we dismiss Petitioner's motion to dismiss the Financial Documents as moot.

2. Exhibits 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, 2278, and portions of Exhibit 2059 (¶¶ 61, 73, 85, 88–94, 98, 99, 103)

Petitioner argues that Exhibits 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, and 2278 (collectively, the "Marketing Exhibits") purport to be Patent Owner's supportive internal marketing materials and ATU survey data. Pet. Mot. Exclude 6. Petitioner contends that Patent Owner offers the Marketing Exhibits as evidence of the claimed methods commercial success and as objective indicia of non-obviousness. Petitioner states that it timely objected to the challenged Marketing Exhibits. *Id.* (citing Papers 23, 48).

Petitioner urges us to exclude the Marketing Exhibits under FRE 403 because their probative value is substantially outweighed by the dangers of unfair prejudice, confusion, and misleading the factfinder.

As in Section III.A.1 above, we do not reach Patent Owner's arguments that the challenged claims are non-obvious (Grounds 4–6), because we conclude that they are anticipated by Dixon (Ground 1). *Cohesive Techs.,* 543 F.3d at 1364. We consequently dismiss Petitioner's motion to exclude the Marketing Exhibits as moot.

3. Exhibits 2079, 2080, 2084, and 2085

Petitioner argues that Exhibits 2079, 2080, 2084, and 2085 (the "Sequence Exhibits") are webpage printouts of the amino acid sequences of human VGFR1 and VGFR2 that should be excluded under FRE 402 and FRE 403. Pet. Mot. Exclude 8. Petitioner contends that Patent Owner's expert, Dr. Klibanov, offers the Sequence Exhibits as evidence of variability in publicly available amino acid sequences of human VGFR1/2. *Id.* (citing,

e.g., Ex. 2057 ¶¶ 76, 78, 79, 82, 86, and 87). Petitioner states that it timely objected to the Sequence Exhibits. *Id.* (citing Paper 48).

Petitioner argues that Exhibits 2079 and 2084 are webpage printouts dated February 28, 2023, that should be excluded as irrelevant non-prior art under FRE 402, and as unfairly prejudicial under FRE 403. Pet. Mot. Exclude 8–9. Petitioner asserts that Exhibits 2079 and 2084 indicate on their faces that they were both printed on February 28, 2023, twelve years after the alleged priority date of the challenged patent, and therefore have no bearing on the patentability of the challenged claims. *Id.* at 9. Petitioner also contends that Patent Owner fails to cite Exhibits 2079, 2080, 2084, and 2085 in its Preliminary Response, Response, or Sur-Reply, demonstrating that they do not have a tendency to make any fact of consequence more or less probable. *Id.* (citing *SK Innovation Co., Ltd. v. Celgard, LLC*, IPR2014-00679, Paper 58, 49 (PTAB September 25, 2015).

Patent Owner responds that the data contained within the Sequence Exhibits antedates the priority date of the '681 patent, i.e., January 13, 2011. PO Opp. Mot. Exclude 8. Patent Owner asserts that Exhibits 2080 and 2085 indicate that they were publicly available as of January 11, 2011. *Id.* (citing Ex. 2080, 1; Ex. 2085, 1). Patent Owner argues that Exhibit 2079 provides the same accession number or identifier, "P17948," and the same title, "VGFR1_HUMAN," and contains the same sequence information as Exhibit 2080, which Patent Owner asserts was publicly available before the priority date. *Id.* (citing Ex. 2079, 9; Ex. 2080, 3). Patent Owner makes corresponding arguments for Exhibits 2084 and 2085. *Id.*

Patent Owner also disputes Petitioner's argument that the Sequence Exhibits are not cited in Patent Owner's Response. PO Opp. Mot. Exclude

10. Patent Owner points to the testimony of Dr. Klibanov, who cites to the Sequence Exhibits, among other exhibits (citing PO Resp. 27 (citing Exs. 2078–2086), also citing *id.* at 26, 27, 29–30, 32).

Petitioner disputes Patent Owner's contention that the information contained in Exhibits 2079 and 2084 was available, in the form of Exhibits 2080 and 2085, before the '681 patent's claimed priority date of January 13, 2011. Pet. Reply Mot. Exclude 3. Petitioner also contends that Exhibits 2079 and 2084 are duplicative of Exhibits 2080 and 2085 and should be excluded under FRE 403 as needlessly cumulative. *Id.* Furthermore, argues Petitioner, to the extent they are not cumulative, they should be excluded because Patent Owner has provided no evidence that the information was available prior to January 13, 2011. *Id.* (citing *In re Lister*, 583 F.3d 1307, 1316 (Fed. Cir. 2009).

Petitioner also asserts that, in arguing the relevance of the Sequence Exhibits, Patent Owner cites to a single sentence in the Response in which the four exhibits in question are among nine that are not themselves directly referenced, but merely cited in Dr. Klibanov's Declaration. Pet. Reply Mot. Exclude 4 (citing PO Resp. 27). Petitioner contends that, because this sentence is the only instance Patent Owner relies on for the Sequence Exhibits, they are not relevant to any issue before the Board and should be excluded under FRE 401 and 402. *Id.*

We are not persuaded by Petitioner's arguments. Exhibits 2079 and 2080 both identify the sequences for VGFR1 (accession no. P17948) presented in each as having the same accession number, P17948, and Exhibit 2080 expressly identifies the entry date of the sequence into the Uniprot protein sequence and functional information database as at least January 11,

2011, which antedates the claimed priority date of the '681 patent. *See* Ex. 2057, 79 (Dr. Klibanov testifies as to the date). Exhibit 2079 provides further identifying information of the sequence identified in the two Exhibits. The two Exhibits thus complement each other, each providing additional information about the other, and indicating an entry date of the sequence as prior to the priority date of the '681 patent. The same is true for Exhibits 2084 and 2085 with respect to VGFR2 (accession no. P35968). Petitioner does not contest that the database was publicly available, and we conclude that the evidence is relevant prior art.

With respect to Petitioner's arguments that the Sequence Exhibits are unduly duplicative, we do not find that a pair of exhibits documenting the amino acid sequence of two proteins relevant to the claimed sequence is unduly cumulative, particularly given the complementary natures of Exhibit 2079 with Exhibit 2080, and Exhibit 2084 with Exhibit 2085. As to the extent of Patent Owner's reliance on the Sequence Exhibits, given the relevance of the Exhibits, we find this argument goes more to the weight of the evidence, rather than its admissibility. We consequently deny Petitioner's motion to exclude the Sequence Exhibits.

4. Exhibits 2098, 2101, 2103, 2104, 2122, 2298, and 2299

a. Exhibit 2098

Petitioner argues that Patent Owner does not cite Exhibit 2098 in its Preliminary Response, Response, or Sur-Reply, and that it is therefore not relevant to any contested issue in this proceeding. Pet. Mot. Exclude 9 (citing FRE 402). Petitioner also asserts that Exhibit 2098 is dated March 14, 2014, and Patent Owner filed it under seal. *Id.* at 10. As such, argues

Petitioner, Exhibit 2098 was not publicly available prior art. *Id.* (citing *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1568–69 (Fed. Cir. 1988).

Patent Owner responds that Exhibit 2098 was cited and relied on by Dr. Klibanov, Patent Owner's expert, and in Patent Owner's Response, through citation to the relevant paragraph of Dr. Klibanov's report. PO Opp. Mot. Exclude 9 (citing PO Resp. 39 (citing Ex. 2057 ¶ 120)). Patent Owner contends that it does not rely upon Exhibit 2098 as prior art, but rather to illustrate the inherent variability in the production of VEGF Trap-Eye, and that this variability was known in the prior art. *Id*. (citing PO Resp. 39–40 (citing Ex. 2057 ¶¶ 117–120); *see also id.* at n.6 (citing Exs. 2096, 2097, 2099, 2100)).

We are not persuaded by Petitioner's argument that Exhibit 2098 should be excluded. Paragraphs 117–119 of the Klibanov Declaration are offered by Patent Owner to demonstrate that it was known in the prior art that synthesis of recombinant human proteins was known to be inherently variable. *See* Ex. 2057 ¶¶ 117–119 (citing e.g., Ex. 2096, 91; Ex. 2097, 4). Exhibit 2098, although not publicly-available prior art, is at least probative of the understanding of one of ordinary skill in the art and, in consequence, admissible. We therefore deny Petitioner's motion to exclude Exhibit 2098.

b. Exhibit 2101

Petitioner next urges us to exclude Exhibit 2101. Petitioner argues that Exhibit 2101, a non-public, internal, technical report, was not cited by Patent Owner in its Preliminary Response, Response, or Sur-Reply, and that it is therefore not relevant to any contested issue in this proceeding under

FRE 402. Pet. Mot. Exclude 10. Petitioner also argues that Exhibit 2101 should be excluded as irrelevant non-prior art. *Id.* (citing FRE 402).

Petitioner contends that Exhibit 2101 should also be excluded under FRE 801–803 as constituting inadmissible hearsay evidence. Pet. Mot. Exclude 10. According to Petitioner, Exhibit 2101 includes out-of-court statements of PO's in-house personnel, offered for the truth of the matters asserted therein. *Id.*

Patent Owner responds that it does not rely on Exhibit 2101 for its prior art teaching; rather, Patent Owner asserts, Exhibit 2101 illustrates the inherent variability in producing VEGF Trap-Eye, which was known in the prior art. PO Opp. Mot. Exclude 10 (citing Ex. 2057 ¶¶ 121–131); PO Resp. 39–40); *see, e.g.*, Ex. 2057, 119 (citing Ex. 2096, 91; Ex. 2097, 4)).

Patent Owner also disputes Petitioner's assertion that Exhibit 2101 contains inadmissible hearsay evidence. PO Opp. Mot. Exclude 11. According to Patent Owner, Ms. Weber's Declaration testimony demonstrates that Exhibit 2101 falls within the business records exception to hearsay, as set forth in FRE 803(6): it is a scientific report, was stored on Regeneron servers, and bears facial indications of trustworthiness (written on Regeneron letterhead and dated and signed by Dr. Koehler-Stec, a study director and Regeneron employee). *Id.* (citing Ex. 2049, 24–26). Patent Owner notes that Petitioner does not challenge the foundation laid for the business records exception, and does not identify any condition of FRE 803(6) that has not been met. *Id.*

Patent Owner relies upon Exhibit 2049 (the purported testimony of "Ms. Weber") as authenticating Exhibit 2101 and demonstrating that it falls within the business records exception. PO Opp. Mot. Exclude 11. However,

there is no Exhibit 2049[11] entered into evidence in this *inter partes* review, nor can we readily discern within the record an exhibit that purports to provide the authenticating foundation Patent Owner relies upon.

Rule 803(6) allows business records to be admitted "if witnesses testify that the records are integrated into a company's records and relied upon in its day to day operations." *Air Land Forwarders, Inc. v. United States*, 172 F.3d 1338, 1342 (Fed. Cir. 1991) (quoting *Matter of Ollag Constr. Equip. Corp.*, 665 F.2d 43, 46 (2d Cir. 1981). Absent any such authenticating witness foundation, we cannot conclude that Exhibit 2101 falls within the Business Records exception of FRE 803(6), and we grant Petitioner's motion to exclude Exhibit 2101 as containing inadmissible hearsay.

c. Exhibit 2122

Petitioner next argues that Exhibit 2122, a confidential (filed under seal), non-public excerpt of clinical study protocol VGFT-OD-0605, should be excluded under FRE 402, 403, and 802. *See* Pet. Mot. Exclude 11. Petitioner first argues that Exhibit 2122 is irrelevant non-prior art under FRE 402 and unfairly prejudicial under FRE 403. *Id.* Petitioner argues that Patent Owner's sealed filing of Exhibit 2122 confirms it was not publicly available, and therefore does not demonstrate the POSA's knowledge or a prior art teaching. *Id.* Petitioner contends that any probative value of the

[11] Nor can we find a corresponding Exhibit 2049, or readily discern an exhibit that could reasonably be construed as providing the evidence of the missing Exhibit 2049, in the related IPR2022-01226, which was argued at the same time as the present *inter partes* review.

Exhibit is substantially outweighed by the dangers of unfair prejudice, confusion, and misleading the factfinder. *Id.*

Petitioner also argues that the reliance of Patent Owner's expert, Dr. Do, to assert as true the statements made in Exhibit 2122 constitutes impermissible hearsay evidence. Pet. Mot. Exclude 11–12 (citing Ex. 2056 ¶ 116).

Patent Owner argues, *inter alia*, that Ms. Weber's testimony makes clear that Exhibit 2122 falls within FRE 803(6), the business records exception to the rule against hearsay: it is a clinical study protocol, stored in Regeneron's regulatory archive, and bears facial indicia of trustworthiness (Regeneron protocol headers and file path information on each page). PO Opp. Mot. Exclude 12 (citing Ex. 2048 ¶ 3; Ex. 2049, 24–26).

Patent Owner again relies on an Exhibit (Ex. 2048) to support the assertion that Exhibit 2122 falls within the Business Records exception of FRE 803(6). Again, however, no such Exhibit 2048 is present in the record of this *inter partes* review, nor can we readily discern within the record an exhibit that purports to provide the authenticating foundation Patent Owner relies upon. *See Air Land*, 172 F.3d at 42. In the absence of any such authentication, we consequently grant Petitioner's motion to exclude Exhibit 2122 as impermissible hearsay under FRE 803.

d. Exhibit 2103 and Exhibit 2104

Petitioner contends that these Exhibits are confidential (filed under seal), non-public documents purported to be a research collaboration agreement and email chain and should be excluded under FRE 402, 403, and 802. Pet. Mot. Exclude 12. Petitioner argues that Exhibits 2103 and 2104

should be excluded as irrelevant non-prior art under FRE 402 and unfairly prejudicial under FRE 403. *Id.* Petitioner also argues that the Exhibits are hearsay under FRE 801, and should be excluded. *Id.*

Patent Owner responds that, although Patent Owner does not use Exhibits 2103 and 2104 as prior-art, and because non-prior art may be relevant, Petitioner's argument lacks merit for the same reasons as discussed with respect to Exhibit 2101. PO Opp. Mot. Exclude 12; *see supra* Section III.A.4.b.

Patent Owner additionally argues that Jeffrey Spada, Associate Director, eDiscovery and Litigation Support at Regeneron Pharmaceuticals, Inc., authenticated these documents in his sworn declaration and during his deposition. PO Opp. Mot. Exclude 12 (citing Ex. 2343 ¶¶ 1–3; Ex. 2349, 13–14, 15–16, 16–18, 20, 21). According to Patent Owner, Mr. Spada's testimony establishes that Exhibits 2103 and 2104 fall within FRE 803(6), the business records exception to the rule against hearsay: they are a Regeneron research collaboration agreement and an email chain regarding the same, stored in the custodial files of George Yancopoulos, the inventor of the '681 patent, and bear facial indicia of trustworthiness. *Id.* at 12–13 (citing Ex. 2343 ¶¶ 1–3; Ex. 2349, 13–14, 15–16, 16–18, 20, 21).

In its Response, Patent Owner offers the Exhibits as part of its argument that the amino acid sequence of VEGF Trap-Eye was not publicly available before EYLEA's FDA approval in November 2011. *See* PO Resp. 25. Specifically, Patent Owner points to Exhibits 2103 and 2104 as evidence that Patent Owner imposed restrictions on its research collaborators receiving VEGF Trap samples for experimentation purposes. *Id.* at 25–26 (citing Ex. 2103 § 5 Agreement; Ex. 2104).

We agree with Patent Owner that Ex. 2103 and 2104 are relevant to Patent Owner's argument that persons of ordinary skill in the art would not have had access to the VEGF Trap-Eye sequence at the time of invention. As such, we conclude that they are relevant under FRE 402 and 403.

We have reviewed the Declaration and relevant foundational testimony of Mr. Spada, and conclude that he has satisfactorily established that Exhibits 2103 and 2104 fall within the business records exception of FRE 803(6) as a record normally kept in the course of a regularly conducted business activity.[12] We therefore deny Petitioner's motion to exclude Exhibits 2103 and 2104.

e. Exhibits 2298 and 2299

Petitioner next argues that Exhibit 2298, a confidential (filed under seal), non-public document alleged to be a clinical study agreement between Vitreoretinal Consultants and Patent Owner, should be excluded because Patent Owner does not cite to Exhibit 2298 in its Preliminary Response, Response, or Sur-Reply, and is consequently inadmissible under FRE 401–

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[12] Federal Rule of Evidence 803(6) states that:

> Records of regularly conducted activity. A memorandum, report, record, or data compilation, in any form, of acts, events, conditions, opinions, or diagnoses, made at or near the time by, or from information transmitted by, a person with knowledge, if kept in the course of a regularly conducted business activity, and if it was the regular practice of that business activity to make the memorandum, report, record or data compilation, all as shown by the testimony of the custodian or other qualified witness, unless the source of information or the method or circumstances of preparation indicate lack of trustworthiness.

See Shu-Hui Chen v. Bouchard, 347 F.3d 1299, 1308 n.2 (Fed. Cir. 2003)

402. Pet. Mot. Exclude 13. Similarly, Petitioner contends that Exhibit 2299, a confidential (filed under seal), non-public compilation of the VIEW protocol signature pages, should be excluded because it was not publicly available, and does not represent a person of ordinary skill in the art's knowledge or a prior art teaching. *Id.* at 13–14. Petitioner also contends that Patent Owner also fails to cite Exhibit 2299 in its Preliminary Response, Response, or Sur-Reply, and is consequently inadmissible under FRE 401–402. *Id.* at 13.

Petitioner additionally argues that Exhibit 2299 is inadmissible as hearsay evidence because the papers are out-of-court statements offered for the truth of the matter asserted, i.e., the alleged confidentiality restrictions in place as of July 2007 regarding VEGF Trap-Eye. Pet. Mot. Exclude 13.

Patent Owner responds that Dr. Brown relies on Exhibit 2298 in his Declaration, and that declaration paragraph is cited in Patent Owner's Response. PO Opp. Mot. Exclude 13 (citing PO Resp. 25 (citing Ex. 2055 ¶ 67)).

With respect to Exhibit 2299, Patent Owner contends that Dr. Brown's and Ms. Weber's testimony establish that Exhibit 2299 falls within FRE 803(6), the Business Records exception to the hearsay rule. PO Opp. Mot. Exclude 14. According to Patent Owner, the Exhibit was generated in the ordinary course of regularly conducted business activity (i.e., a clinical investigation), was stored by Regeneron in its regulatory archives and by Dr. Brown's practice at Iron Mountain, and bears facial indications of trustworthiness (dated signatures by Dr. Brown's partner on every page), all as confirmed by individuals with knowledge. *Id.* (citing Ex. 1022, 62–63).

In his Declaration, Dr. Brown testifies that:

> [M]y institution, Vitreoretinal Consultants of Houston, signed a Clinical Study Agreement to conduct a clinical study entitled "A Randomized, Double Masked, Active Controlled Phase III Study of the Efficacy, Safety, and Tolerability of Repeated Doses of Intravitreal VEGF Trap in Subjects with Neovascular Age-Related Macular Degeneration" concerning Protocol number VGFT-OD-0605, which required my institution/practice to maintain information disclosed by Regeneron or generated as a result of the study in confidence and also limited our use of such information only for the purposes of the study. Ex. 2298 ¶ 6. In addition to the clinical study agreement, when our group/institution was provided the protocol for the VIEW trial, the document was clearly marked with a confidentiality legend and required that the clinical investigator sign the protocol and agree to be bound by its limitations on use and disclosure. Ex. 2299.

Ex. 2055 ¶ 67. Patent Owner relies upon this testimony as demonstrating that the amino acid sequence of VEGF Trap-Eye (the claimed SEQ ID NO:1 and SEQ ID NO:2) was not known to the artisan of ordinary skill, and that the clinical users of the drug were subject to confidentiality restrictions. *See* PO Resp. 25–26. As such, we find that the evidence adduced in these Exhibits is relevant to Patent Owner's arguments.

With respect to Petitioner's argument that Exhibit 2099 constitutes inadmissible hearsay evidence, and as we have explained above, we can find no evidence of an Exhibit 2048 or 2049, or of Ms. Weber's testimony, in Patent Owner's exhibits of record in this *inter partes* review. However, we find that the testimony of Dr. Brown is sufficient to authenticate the Exhibit and to establish that it falls within the Business Records exemption of FRE 803(6). Therefore, we find that Exhibits 2298 and 2299 are admissible.

Petitioner's motion to exclude Exhibits 2298 and 2299 is consequently denied.

f. Portions of Exhibits 2055–57, and 2059

Finally, Petitioner argues that Patent Owner's expert declaration testimony corresponding to the Challenged Exhibits should also be excluded. Pet. Mot. Exclude 14 (citing *Wi-LAN Inc. v. Sharp Elecs. Corp.*, 992 F.3d 1366, 1374 (Fed. Cir. 2021). Petitioner contends that Patent Owner has adduced no evidence that any of the challenged Exhibits are documents upon which a person of ordinary skill in the art would "reasonably rely" in forming an opinion on the subject matter at issue, thus warranting exclusion of portions of the declarations of Dr. Do (Ex. 2056 ¶ 116), Dr. Klibanov (Ex. 2057 ¶¶ 76, 78–79, 82, 86, 120–21, 123–28), Dr. Brown (Ex. 2055 ¶ 67), and Dr. Manning (Ex. 2059 ¶¶ 11, 28–29, 43, 47–117).

Patent Owner responds that Petitioner's motion fails to identify which declaration paragraphs correspond to which exhibits, or to explain how or why the experts' use of any particular exhibit is allegedly improper. PO Opp. Mot. Exclude 14. Patent Owner contends that Petitioner's assertions lack particularity and do not satisfy Petitioner's burden on a motion to exclude. *Id.*

Patent Owner also argues that Petitioner's original objections to evidence failed to identify the portions of the expert declarations that it now moves to exclude with any particularity, instead asserting only that the FRE 703 objection applies to each of Exhibits 2048, 2049, 2050, and 2052 in their entirety. PO Opp. Mot. Exclude 15 (citing Pet. Mot. Exclude 3; and

citing *Nippon Suisan Kaisha Ltd. v. Pronova Biopharma Norge AS*, PGR2017-00033, 2019 WL 237114, at *23–24 (PTAB Jan. 16, 2019).

As we explained above, we dismiss Petitioner's motion to exclude the Financial Exhibits and the Marketing Exhibits as moot. We consequently also dismiss as similarly moot, Petitioner's motion to exclude Dr. Manning's related testimony. (Exhibit 2059 ¶¶ 11, 28–29, 43, 47–117).

Because we have denied Petitioner's motion to exclude the Sequence Exhibits, we also deny Petitioner's motion to exclude the related portions of Dr. Klibanov's testimony (Ex. 2057 ¶¶ 76, 78, 79, 82, and 86). Similarly, because we deny Petitioner's motion to exclude Exhibits 2098, we deny Petitioner's motion to exclude the related testimony of Dr. Klibanov with respect to that Exhibit (Ex. 2057 ¶ 120).

We have also explained why we deny Petitioner's motion to exclude Exhibit 2299. We therefore also deny Petitioner's motion to exclude the related foundational testimony of Dr. Brown (Ex. 2055 ¶ 67).

We grant Petitioner's motion to exclude the unauthenticated Exhibit 2101 as inadmissible hearsay evidence, as explained above. We therefore also exclude the related portions of Dr. Klibanov's testimony that rely upon that evidence relating to the Regeneron study (Ex. 2057 ¶¶ 123–128).

Finally, we also grant Petitioner's motion to exclude Exhibit 2122 under FRE 803. We therefore also exclude the related testimony of Dr. Do (Ex. 2056 ¶ 116).

5. Summary

For the reasons we have explained in the preceding sections, we dismiss as moot Petitioner's motion to exclude the Financial Exhibits

(Exs. 2037, 2038, 2169, 2170, 2200, 2218, 2229, 2279, and 2282–85) and Marketing Exhibits (Exs. 2039, 2136, 2138–40, 2163, 2176, 2190, 2197, 2208, 2243, 2244, 2250, 2259, 2277, and 2278) as well as Dr. Manning's related testimony (Ex. 2059 ¶¶ 11, 28–29, 43, 47–117).

We deny, for the reasons explained above, Petitioner's motion to exclude the Sequence Exhibits (Exs. 2079, 2080 2084, and 2085) as well as Exhibits 2098, 2103, 2104, 2228, and 2229. We similarly deny Petitioner's motion to exclude the portions of Patent Owner's expert's testimony related to these Exhibits, *viz.*, that of Dr. Klibanov (Ex. 2057 ¶¶ 76, 78, 79, 82, 86, 120).

We grant Petitioner's motion to exclude Exhibits 2101 and 2122. We also grant Petitioner's motion to exclude the related portions of Dr. Klibanov's and Dr. Do's testimony relying upon those Exhibits (Ex. 2057 ¶¶ 123–128 and Ex. 2056 ¶ 116, respectively).

B. Patent Owner's Motion to Exclude

Patent Owner moves to exclude Exhibits 1058, 1020, 1087, 1167, 1124, 1150, and 1151, and related portions of Exhibits 1102, 1103, 1107, and 1115. PO Mot. Exclude 1, 10. We consider each of Patent Owner's arguments in turn.

a. Ex. 1058

Patent Owner argues that Ex. 1058 should be excluded as evidence. PO Mot. Exclude 2. Exhibit 1058 (Rosenfeld) forms a partial basis for Petitioner's Ground 5 contentions that the challenged claims are unpatentable as obvious over the cited prior art. *See* Pet. 13.

Patent Owner argues that: (1) Ex. 1058 is not authenticated and irrelevant under FRE 401-403, 802, and 901. PO Mot. Exclude 2–9.

As we explain below, we conclude that the challenged claims in this *inter partes* review are anticipated by Dixon and therefore unpatentable (Ground 1). Because we reach this conclusion, we do not reach Petitioner's contentions that the claims are obvious on the basis of Ground 5. Nor does our analysis rely upon, or cite to, Exhibit 1058. We consequently dismiss as moot Patent Owner's motion to exclude Exhibit 1058.

b. Exhibits 1020, 1087, 1167, and related portions of Exhibits 1102, 1103, 1107, and 1115

Patent Owner next urges us to exclude Exhibits 1020, 1087, and 1167 on the basis that none of these Exhibits were cited in the Petition or the Petitioner's Reply. PO Mot. Exclude 10. Similarly, Patent Owner seeks to exclude the related portions of Petitioner's expert testimony not cited in the pleadings:

(i) Ex. 1002 ¶¶ 30–42, 46–47, 53–63, 65–69, 71–82, 101, 109–112, 114, 119, 122–125, 129–131, 133–134, 137, 313-–331, 335–346, 356–372, 377–389, 393, and 396;

(ii) Ex. 1003 ¶¶ 31–43;

(iii) Ex. 1107 ¶¶ 6–48, 51–64, 66–71, 78–86, 92–96, and 101–27;

(iv) Ex. 1115 ¶¶ 21, 23–59.

Id. Patent Owner states that it timely objected to each of these uncited exhibits and expert declaration paragraphs. *Id.* Patent Owner contends that these uncited exhibits and testimony were not relied upon by Petitioner and should therefore be excluded as irrelevant. *Id.* at 11.

Petitioner responds that Patent Owner's contention that multiple portions of at least Exhibits 1002, 1107, and 1115 "were not cited in the

pleadings" is inaccurate. Pet. Opp. Mot. Exclude 8–9 (quoting PO Mot. Exclude 10). Petitioner asserts that its Reply does in fact rely upon at least paragraph 73 of Exhibit 1002 to rebut Regeneron's assertion of "great uncertainty" regarding extended dosing in clinical practice prior to 2010. *Id.* at 9 (citing Pet. Reply 60, 22). Petitioner also contends that its Reply further relies on at least paragraphs 14–44, 51–57, and 102–126 of Exhibit 1107 to explain: (1) alleged shortcomings of the intrinsic record; (2) Patent Owner's representations to the U.S. Patent and Trademark Office; (3) the realities of the VIEW clinical trials; and (4) secondary consideration of non-obviousness analyses. *Id.* (citing Pet. Reply 5, 8, 23, 25, 8, 11). Petitioner argues that its Reply also relies on paragraphs 28–59 of Exhibit 1115 in its blocking patent discussion. *Id.* (citing Pet. Reply 23).

Petitioner additionally argues that the identified exhibits and expert testimony are a matter of public record, and the Board may have reason to consult any of these exhibits or take public notice of them. Pet. Opp. Mot. Exclude 9. Petitioner notes that Patent Owner has provided no legitimate justification for excluding this evidence altogether at this time. Petitioner argues that the Board can, in its discretion, assign weight to the evidence as appropriate, and as it has done in prior IPRs. *Id.* (citing, e.g., *Square, Inc. v. 4361423 Canada Inc.*, IPR2019-01649, Paper 43, 32–33 (PTAB Apr. 22, 2021).

Patent Owner replies that Petitioner does not deny that Exhibits 1020, 1087, 1167, and the challenged portions of Exhibits 1002, 1003, 1107, and 1115 not cited by Petitioner in its Opposition were not relied upon in any of its pleadings. Patent Owner contends that these Exhibits and portions of Exhibits should be excluded as being of no consequence in determining the

outcome of the proceeding. PO Reply Mot. Exclude 3–4 (citing *One World Techs., Inc. v. Chamberlain Grp., Inc.*, IPR2017-00126, Paper 56 at 16 (PTAB Oct. 24, 2018)).

We do not find Patent Owner's argument persuasive. To the extent that the challenged Exhibits and testimony are relied upon in this Final Written Decision, the Board is capable of assigning to them appropriate probative weight. *See, e.g.*, *Square, Inc. v. 4361423 Canada Inc.*, IPR2019-01649, Paper 43, 32-33 (PTAB Apr. 22, 2021). Moreover, Patent Owner alleges no prejudice by the inclusion of these Exhibits and testimony in the record of this *inter partes* review. Because Board proceedings favor inclusion in the public record, and because Patent Owner alleges no potential prejudice from inclusion of this evidence in the record, we deny Patent Owner's motion to exclude Exhibits 1020, 1087, and 1167 and the challenged paragraphs of Exhibits 1102, 1103, 1107, and 1115.

c. Exhibits 1124, 1150, and 1151

Patent Owner next seeks to exclude Exhibits 1124, 1150, and 1151. PO Mot. Exclude 14. These Exhibits consist of complaints and exhibits filed by the U.S. Department of Justice and Horizon Healthcare Services, Inc. against Patent Owner and were introduced by Petitioner to impeach the credibility of Patent Owner's commercial success expert, Dr. Manning. *See* Pet. Opp. Mot. Exclude 10–11. Patent Owner contends that these Exhibits are irrelevant, prejudicial, and inadmissible hearsay evidence under FRE 403 and FRE 803, 804, and 807. PO Mot. Exclude 12–14.

Dr. Manning's testimony relates to the commercial success of the compound recited in the challenged claims as objective evidence of non-

obviousness. As we explained above, we conclude in this Final Written Decision is anticipated by Dixon (Ground 1) and we do not reach Petitioner's obviousness Grounds 4–6. We therefore do not rely upon Dr. Manning's testimony as to objective indicia of non-obviousness. *See Cohesive Techs.,* 543 F.3d at 1364. Nor does our analysis rely upon, or cite to, the Exhibits challenged by Patent Owner. Consequently, we dismiss as moot, Patent Owner's motion to exclude Exhibits 1124, 1150, and 1151.

d. Summary

For the reasons set forth above, we dismiss Patent Owner's motion to exclude Exhibits 1058, 1124, 1150, and 1151. We deny Patent Owner's motion to exclude Exhibits 1020, 1087, 1167, and the related portions of Exhibits 1102, 1103, 1107, and 1115 cited by Patent Owner.

IV. ANALYSIS

A. Claim Construction

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b) (2020). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006)

(citing *Phillips*, 415 F.3d at 1312–17). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

Petitioner initially argues that the language of the preamble reciting "a method for treating" is not limiting upon the claims. Pet. 17–20. Petitioner additionally proposes constructions for the claim terms "initial dose," "secondary dose," and "tertiary dose." *Id.* at 24–25. Finally, Petitioner argues that the limitation reciting "wherein exclusion criteria for the patient include all of…." (the "exclusion criteria") are not entitled to patentable weight under the printed matter doctrine. *Id.* at 25–28.

Patent Owner disagrees, arguing that not only is the preamble limiting and requires "treating," but that the recited "method for treating" requires "a high level of efficacy." PO Resp. 8–19. Patent Owner further argues that the printed matter doctrine is inapplicable to the "exclusion criteria" limitation and that exclusion criteria are limiting upon the claims. *Id.* at 18–25. We address each of these arguments in turn.

1. Preamble

a. Petitioner's arguments

Petitioner argues the preamble is not limiting upon the claims. Pet. 17–18. Petitioner argues that: (1) the preamble is merely a statement of intended purpose and, therefore, not a limitation; and (2) the preamble provides no antecedent basis for any other claim element, and that any argument that "the patient" and "angiogenic eye disorder" claim terms find their respective meaning in the preamble is meritless. *Id.* at 20.

Alternatively, argues Petitioner, if the preamble is limiting, it should be given its plain and ordinary meaning, which does not require any specific efficacy requirement. *Id.* at 20–23.

b. Patent Owner's Response

Patent Owner responds that: (1) the preamble is limiting and requires "treating"; (2) the recited "method for treating" requires a high level of efficacy; and (3) the intrinsic record supports a high level of efficacy. PO Resp. 8–18.

Specifically, Patent Owner argues that where our reviewing court has found "method for treating" preambles to be limiting, they have consistently found that such claims require effective treatment. PO Resp. 9 (citing, e.g., *Sanofi Mature IP v. Mylan Labs. Ltd.*, 757 F. App'x 988, 992–94 (Fed. Cir. 2019); *Eli Lilly & Co. v. Teva Pharms. Int'l GMBH*, 8 F.4th 1331, 1340–43 (Fed. Cir. 2021)). Patent Owner disputes the Board's conclusion in the -00881 IPR that the claimed methods encompass ineffective administration, citing the '681 Specification's disclosure that "[t]he amount of VEGF antagonist administered to the patient in each dose is, in most cases, a therapeutically effective amount." *Id.* (quoting Ex. 3001, 10). Patent Owner contends that the -00881 Decision's reliance on that passage is "contrary not only to the above precedent, but also the weight of evidence." *Id.* (citing Ex. 2056 ¶¶ 59–67; Ex. 2021, 192–193, 200). According to Patent Owner, a person of ordinary skill in the art would not look at this passage in isolation and, asserts that the remainder of the Specification "repeatedly characterizes the method as one that is useful for treating angiogenic eye disorders in patients." *Id.* at 9–10 (quoting Ex. 3001, 19).

Patent Owner argues further that the claimed method for treating requires a high level of efficacy. PO Resp. 10. According to Patent Owner, the method of the '681 patent was groundbreaking because it maintained initial gains with less frequent "tertiary doses." *Id.* at 12 (citing Ex. 1001, col. 2, ll. 7–24). Patent Owner contends that, contrary to Petitioner's suggestion that this high level of efficacy lacks support, every exemplification of the claimed Q8 dosing regimen in the '681 patent specification shows the regimen achieving and maintaining a high level of efficacy in the treated population. *Id.* at 14 (citing Pet. 22; also citing, e.g., Ex. 1001, Examples 4, 5).

Patent Owner points to Shams[13], an abandoned patent publication, which discloses an extended dosing regimen for Lucentis that meets the operative steps of the '681 patent claims (Q8 or longer tertiary dosing), where study subjects gained vision during monthly loading doses but lost those gains during tertiary maintenance dosing. PO Resp. 13 (citing Ex. 2022, 30–32, 40–42, 44–45, 46–47, 48–49, 561; Ex. 1030, 7–9, Fig. 1C). Patent Owner asserts that, by expressly recognizing that the PIER dosing regimen left an unmet need in the art, the '681 Specification makes clear that achieving and maintaining a high level of efficacy is the whole point of the claimed methods. *Id.*

Patent Owner argues that a person of ordinary skill in the art would not have required non-inferiority data for every angiogenic eye disorder to understand, from the disclosures of the '681 patent, that VEGF Trap would be similarly effective across angiogenic eye disorders. PO Resp. 14 (citing

[13] Shams (US 2007/0190058 A1, August 16, 2007) ("Shams") (Ex. 2024).

Pet. 2, 22 n.7; Ex. 2001 ¶¶ 37–38). Patent Owner contends that, once VEGF Trap was shown to be non-inferior to Lucentis in treating wet AMD, a skilled artisan would have expected it to also be highly effective for other angiogenic eye disorders. *Id.* at 15.

Patent Owner also points to the prosecution history of the '681 patent, in which Patent Owner overcame a double patenting rejection to the challenged claims by explaining that the "treatment protocol" encompassed by the claimed invention resulted in surprising efficacy, i.e., noninferiority to ranibizumab, despite less frequent dosing. PO Resp. 15 (citing Ex. 1017, 458–63, 484–86 (citing Ex. 1018); also citing *Fenner Invs., Ltd. v. Cellco P'ship*, 778 F.3d 1320, 1322–23 (Fed. Cir. 2015)).

Patent Owner argues that this evidence supports its contention that, as of 2011, a person of ordinary skill in the art would have understood that the claimed "method for treating," must provide highly effective treatment to the patient (on par with the standard-of-care at patent filing). PO Resp. 15–16 (citing Ex. 2001 ¶¶ 32–39; Ex. 2056 ¶¶ 98, 56–98).

c. Analysis

These same arguments were argued and addressed in the prior -00881 Decision. *See* Ex. 3001, 12–23. As an initial matter, we are not persuaded by Patent Owner's reliance on *Sanofi* and *Eli Lilly*. *See* PO Resp. 9. In *Sanofi*, a non-precedential decision, the Federal Circuit held that the preamble to the claims at issue, reciting "[a] method of increasing survival comprising administering to a patient in need thereof" was limiting upon the claims, in conformance with the court's prior decisions in *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003) and *Rapoport v.*

Dement, 254 F.3d 1053 (Fed. Cir. 2001). *Sanofi*, 757 F. App'x at 992–93. Furthermore, the court held that, because the preamble was limiting, and recited a "method of increasing survival" the proposed claims would now clearly require "increasing survival." *Id.* at 994. The preamble to claim 1 of the '681 patent, however, recites no such "increase" with respect to efficacy, but merely recites "A method for treating an angiogenic eye disorder in a patient," and the remainder of the claim requires no specific efficacy requirement.

Nor does *Eli Lilly* support Patent Owner's position. In *Eli Lilly*, the court upheld the Board's conclusion that the preamble reciting "a method for treating headache in an individual" was limiting upon the claims. *Eli Lilly*, 8 F.4th at 1343. However, it noted, in upholding the Board's conclusion, the Board also "found that while the claims encompass a clinical result, they do not *require* such a result." *Id.* (emphasis added). We also find that the similar language of the preamble to challenged claim 1 of the '681 patent, although encompassing clinical efficacy, does not require it, let alone a "high degree of efficacy."

In the -00881 Decision, challenged claim 1 of US 9,254,338 B2 (the "'338 patent") recited preamble language identical to that recited in claim 1 of the '681 patent, *viz.*, "a method for treating an angiogenic eye disorder in a patient." *See* Ex. 1001, col. 21, ll. 40–41; Ex. 3001, 7. The Board found that this preamble was limiting upon the remainder of the claim. Ex. 3001, 18. Specifically, the Board found that:

> Here, the claims are directed to methods of administering, i.e., using, a VEGF antagonist for an intended purpose of "treating an angiogenic eye disorder in a patient." The Specification repeatedly characterizes the method as one for treating

> angiogenic eye disorders in patients. Apart from the preamble, the independent claims do not elsewhere recite or indicate any other use for the method steps comprising the administration of a VEGF antagonist. Thus, we determine that the preamble sets forth the essence of the invention—treating an angiogenic eye disorder in a patient.
>
> Additionally, we find that the preamble provides antecedent basis for claim terms "the patient" recited in the body of each independent claim, and "angiogenic eye disorders" recited in dependent claims 6, 7, 18, and 20. Indeed, without the preamble, it would be unclear to whom the doses of VEGF are administered.
>
> Thus, …in view of the evidence of record, namely, the claim language and the written description of the '338 patent, we find that the preambles of method claims 1 and 14 are limiting insofar as they require "treating an angiogenic eye disorder in a patient."

Id. at 17–18 (citations omitted). We adopt this same reasoning here and find that the preamble of claim 1 reciting "[a] method for treating an angiogenic eye disorder in a patient" is limiting.

We do not find persuasive, however, Patent Owner's argument that the preamble's recitation of a "method for treating" requires a high level of efficacy. In the -00881 Decision, the Board rejected Patent Owner's similar argument because it required improperly importing limitations into the claims. *See* Ex. 3001, 22. Specifically, the Board found that:

> [W]hen the Specification explains that "[t]he amount of VEGF antagonist administered to the patient in each dose is, in most cases, a therapeutically effective amount," and discloses that "a therapeutically effective amount can be from about 0.05 mg to about 5 mg," we find that a POSA would have understood that any dosage amount within that range administered according to the invention may, in some cases, result in a detectable improvement in "one or more symptoms or indicia of an angiogenic eye disorder," or be one that "inhibits, prevents, lessens or delays the progression of an angiogenic eye disorder,"

> or it may not. In either event, the VEGF antagonist would have been administered for the purpose of treating the eye disorder. In other words, the method of treating the patient with the eye disorder is performed upon administration of the VEGF antagonist to the patient for the purpose of achieving an improvement or beneficial effect in the eye disorder, regardless whether the dosage amount administered actually achieves that intended result.

Id. at 21–22 (citation omitted). Furthermore, the Board found that:

> Patent Owner proposes that the claims require not only achieving a therapeutically effective result, but more specifically, achieving a "high level of efficacy that was noninferior to the standard of care by the time the patent was filed in 2011." In the Sur-reply, Patent Owner describes a "highly effective treatment for angiogenic eye disorders" as "one that is on par to Lucentis or off-label Avastin and can produce visual acuity gains, not just slow vision losses." The Specification refers to "a high level of efficacy" in one instance, i.e., in the "Background" section. The Specification does not describe there, or elsewhere that "treating," in the context of the claims or in the art, requires achieving a "high level of efficacy" or providing results "on par to Lucentis or off-label Avastin."

Id. at 22 (citations omitted).

We adopt the same reasoning here, and find that, for the purposes of this Decision, the evidence of record and the Specification support construing the preamble's recitation of a "method for treating a patient with an angiogenic eye disorder" as meaning administering a compound, i.e., the recited VEGF antagonist, to such patient for the purpose of improving or providing a beneficial effect in their angiogenic eye disorder. We find that, as in *Eli Lilly*, although the claims "encompass a clinical result, they do not require such a result." *Eli Lilly*, 8 F.4th at 1343. We consequently reject

Patent Owner's argument that the preamble to the challenged claims requires a "high level of efficacy," as proposed by Patent Owner. *See* Ex. 3001, 22.

2. "Initial dose," "Secondary Dose," and "Tertiary Dose"

Petitioner next contends that a person of ordinary skill in the art would understand each of these claim terms as expressly defined in the '681 patent's Specification. Pet. 24. The Specification defines the claim terms as follows:

> The terms "initial dose," "secondary doses," and "tertiary doses," refer to the temporal sequence of administration of the VEGF antagonist Thus, the "initial dose" is the dose which is administered at the beginning of the treatment regimen (also referred to as the "baseline dose") ; the "secondary doses" are the doses which are administered after the initial dose; and the "tertiary doses" are the doses which are administered after the secondary doses. The initial, secondary, and tertiary doses may all contain the same amount of dosing regimens, but will generally differ from one another in terms of frequency of administration.

Ex. 1001, col. 3 ll. 34–44. Petitioner also notes that the Specification further explains that "the immediately preceding dose" means "in a sequence of multiple administrations, the dose of VEGF antagonist which is administered to a patient prior to the administration of the very next dose in the sequence with no intervening doses." Pet. 24 (citing Ex. 1001, col. 3, ll. 54–59; Ex. 1002 ¶¶ 44–45).

We adopt Petitioner's proposed construction of the claim terms "initial dose," "secondary dose," and "tertiary dose." Petitioner proposes adoption of the definitions expressly set forth in the Specification of the '681 patent, *viz.*, that the initial dose is the dose "administered at the beginning of

the treatment regimen," and is followed by the secondary doses that are "administered after the initial dose," and the tertiary doses are "administered after the secondary doses" and may be distinguished from the secondary doses "in terms of frequency of administration." Ex. 1001, col. 3, ll. 36–44.

Patent Owner does not expressly dispute Petitioner's construction, other than to argue that, by 2011, a person of ordinary skill in the art would have understood "initial" and "secondary" doses to correspond to loading doses and "tertiary" doses to correspond to maintenance doses. PO Resp. 11–12 (citing Ex. 2026 ¶¶ 39–40; Ex. 2001 ¶¶ 47–49).

We do not find persuasive Patent Owner's argument that the definition of these terms requires a high, or otherwise defined, degree of efficacy. As we stated in the -00881 Decision:

> Based on those express definitions in the Specification, we do not find cause to construe the terms differently. In particular, we do not find that the Specification requires the "tertiary doses" to maintain any efficacy gain achieved after the initial and secondary doses, or that the term suggests any specific level of efficacy. *The Specification unequivocally states that "[t]he terms 'initial dose,' 'secondary doses,' and 'tertiary doses,' refer to the temporal sequence of administration of the VEGF antagonist."*

Ex. 3001, 25 (emphasis added). We see no need or reason to upend this construction now, and we adopt Petitioner's proposed definition of the claim terms "initial dose," "secondary doses," and "tertiary doses" as the express definition provided by the '681 Specification.

3. <u>The exclusion criteria</u>

The "exclusion criteria" limitation of challenged claim 1 recites:

[W]herein exclusion criteria for the patient include all of:

(1) active intraocular inflammation;

(2) active ocular or periocular infection;

(3) any ocular or periocular infection within the last 2 weeks.

Ex. 1001, col. 21, ll. 58–62.

a. Petitioner's arguments

Petitioner argues that the "exclusion criteria" are entitled to no patentable weight under the printed matter doctrine. Pet. 25.

Petitioner points to the two-part analysis set forth in *Praxair Distrib., Inc. v. Mallinckrodt Hosp. Prods. IP Ltd.*, 890 F.3d 1024, 1032 (Fed. Cir. 2018). Under this analysis we first determine whether the claim limitation in question is directed to printed matter. i.e., "if it claims the content of information." *Praxair*, 890 F.3d 1032 (citing *In re DiStefano*, 808 F.3d 845, 848 (Fed. Cir. 2015). In the second step, we determine whether the printed matter is functionally related to its "substrate," i.e., whether the printed material is "interrelated with the rest of the claim." *Id.* Printed matter that is functionally related to its substrate is given patentable weight. *Id.* (citing *DiStefano*, 808 F.3d at 850).

Petitioner first argues that the exclusion criteria (i.e., preexisting conditions) represent informational content regarding the patient. Pet. 26. Petitioner argues that the challenged claims recite no active step of applying (or assessing the patient for) the exclusion criteria and consequently is "informational content" constituting a "mental step/printed material element." *Id.* at 27. Petitioner asserts that, even if application of the "exclusion criteria" could be inferred, the challenged claims do not dictate

that any procedural step be taken, or that any alteration be made to the claimed dosing regimen. *Id.*

Turning to the second step of the *Praxair* analysis, Petitioner contends that there is no functional relationship between the exclusion criteria and the rest of the claim (i.e., the operative steps of administering a VEGF antagonist to treat an angiogenic eye disorder). Pet. 27. Specifically, Petitioner argues that neither the presence nor absence of any exclusion criteria dictates any changes to the actual claimed dosing steps—i.e., the operative steps remain the same. *Id.* Therefore, argues Petitioner, because the "exclusion criteria" are "directed to mental steps" that "attempt to capture informational content," and lack a functional relationship to the other steps of the claimed treatment method, the exclusion criteria should be "considered printed matter lacking patentable weight." *Id.* (quoting *Praxair*, 890 F.3d at 1033).

b. Patent Owner's Response

Patent Owner contends that the exclusion criteria are entitled to patentable weight. PO Resp. 18. According to Patent Owner, the exclusion criteria are not mere "informational content," and the POSA would understand that they are not optional when practicing the claimed methods. *Id.* at 19 (citing Ex. 2056 ¶ 100). Rather, argues Patent Owner, practicing the challenged claims requires actually applying the recited criteria—i.e., assessing a patient for the conditions listed as exclusion criteria, and administering treatment only to a patient who does not have the recited conditions. *Id.* Patent Owner contends that the plain meanings of the words "exclusion" and "criteria" mandate that patients having the listed conditions

(i.e., the "criteria") are actually "excluded" from treatment. *Id.* at 20 (citing Ex. 2062, 4, 7; Ex. 2056 ¶ 109). Consequently, Patent Owner argues, only patients who are cleared of the exclusion criteria may be treated according to the claimed methods. *Id.*

Patent Owner asserts that the '681 Specification confirms that the exclusion criteria are mandatory. PO Response 20. Patent Owner points to Example 4 of the Specification, which describes 37 exclusion criteria known to have been used in Regeneron's Phase III VIEW clinical trials; numbers 18, 19, and 20 on that list correspond, respectively, to the exclusion criteria of the claims, and were employed in Example 4. *Id.* (citing Ex. 1001, cols. 10–12, ll. 25–62; Ex. 2056 ¶ 107). Patent Owner asserts that Example 4's description is consistent with how the VIEW study exclusion criteria were actually applied: as non-optional criteria that limited the treatment population. *Id.* at 21 (citing Ex. 2056 ¶¶ 103–104, 108).

Patent Owner asserts that both parties' experts confirm that the POSA would understand that the exclusion criteria are mandatory. PO Resp. 21. Patent Owner points to the testimony of Petitioner's expert Dr. Albini, who states that "clinical trial investigators are required to apply each of the exclusion criteria." *Id.* (citing Ex. 1002 ¶¶ 93, 203, 251; Ex. 2323, 105–109). Patent Owner notes that its expert, Dr. Do, agrees. Ex. 2056 ¶¶ 108, 105, 109). Patent Owner contends that the mandatory nature of the exclusion criteria distinguishes them from contraindications printed on a drug label, which a physician may choose to employ, or not. *Id.* (citing Ex. 2056 ¶ 110; Ex. 2323, 103). Contraindications, argues Patent Owner, are "symptom[s], circumstance[s], etc., which tend[] to make a particular course of (remedial) action inadvisable" however it is ultimately at the

clinician's discretion whether to follow them or not. *Id.* at 22 (citing Ex. 2062, 3).

Patent Owner contends that the challenged claims differ markedly from the "printed matter" claims in *Praxair*, which were expressly directed to the provision of "information" or a "recommendation," with no requirement that the "information" or "recommendation" change the scope or practice of the claims. PO Resp. 22 (citing *Praxair*, 890 F.3d at 1029–30*)*. In contrast, asserts Patent Owner, the challenged claims do not recite the provision of information, but instead define which patients are treated by the claimed methods, i.e., patients having an angiogenic eye disorder, and not having any of the exclusion criteria. *Id.* (citing Ex. 1001, claim 1; Ex. 2323, 104–105).

Turning to the second part of the *Praxair* test, Patent Owner argues that the exclusion criteria bear a functional relationship to the claim. PO Resp. 23. Patent Owner asserts that the exclusion criteria define the patient population for treatment, and so define how (i.e., upon whom) the treatment steps are to be performed; ignoring the exclusion criteria would result in a different (broader) group of patients would be treated. PO Resp. 23 (citing PO Prelim. Resp. 40). According to Patent Owner, claim terms defining the population of patients to be treated with a claimed method are limiting. *Id.* (citing, e.g., *Rapoport*, 254 F.3d at 1058–60; *Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d 1349, 1356–57 (Fed. Cir. 2014); *Jansen*, 342 F.3d at 1333–34; *GlaxoSmithKline LLC v. Fibrogen, Inc.*, IPR2016-01318, 2017 WL379248, *3 (PTAB Jan. 11, 2017); *Praxair*, 890 F.3d at 1035).

Patent Owner also contends that the exclusion criteria also require that the medical provider take specific action—assessing the patient for the

exclusion criteria, then administering treatment only to a patient who is determined not to have the excluded conditions. *Id.* (citing Ex. 2056 ¶¶ 101, 105). As an instance of this, Patent Owner points again to Example 4 of the '681 Specification, which discloses that subjects underwent assessment at screening, and that patients who were found to have one of the listed exclusion criteria were excluded from treatment. *Id.* at 23–24 (citing Ex. 2056 ¶¶ 102–104, 108; Ex. 1001, col. 12, ll. 33–62). Patent Owner argues that such assessments are a routine part of clinical practice as well. *Id.* at 24 (citing Ex. 1002 ¶¶ 98, 350; Ex. 2323, 122, 72–82, 92; Ex. 2056 ¶¶ 105, 109).

c. Petitioner's Reply and Patent Owner's Sur-Reply

Petitioner replies that, contrary to Patent Owner's argument, "assessing a patient for the conditions listed as Exclusion Criteria" is not among the claimed steps. Pet. Reply 9. Petitioner points to the District Court's finding in the parallel *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.) (the "district court proceedings") that the claimed exclusion criteria in Patent Owner's related US 10,888,601 and US 11,253,572 patents' (the "'601 and '572 patents") claims lack patentable weight, and observing that "[e]ven under Regeneron's 'assess and exclude' approach, a patient either never starts the method (and hence the method doesn't change); or, if doctors screened for the information and found no infection or inflammation, the same method proceeds." *Id.* (quoting Ex. 1112, 34–35). Petitioner asserts that the "exclusion criteria" are, at most, a non-binding informational "option" for doctors to consider. *Id.* (citing Ex. 1112, 34–35 (citing IPR2022-01226, Institution Decision,

Paper 22, 15 (PTAB Jan. 11, 2023)). Therefore, argues Petitioner, the exclusionary criteria are strictly informational, without requiring the practitioner to act, or refrain from acting, in a specified manner, and not functionally related to the practice of the claimed method. *Id.*

Petitioner also disputes Patent Owner's contention that unlike contraindications printed on a drug label, a skilled artisan would not treat exclusion criteria as optional in clinical practice. Pet. Reply (citing PO Resp. 21). Petitioner points out that Patent Owner's expert, Dr. Do, admits that she "may proceed with the intravitreal injection despite the presence of one of these conditions." *Id.* at 10 (citing Ex. 2056 ¶¶ 158, 110; Ex. 1112, 33. According to Petitioner, Dr. Do also admits that "in the context of a clinical trial, if a patient has one or more of the exclusion criteria, they would not be included in clinical trial," thereby forfeiting treatment, whereas in her own practice she would "exclude the patient from treatment, at least temporarily." *Id.* (citing (Ex. 1109, 149) (Ex. 2056 ¶ 158). Petitioner contends that nothing in the '681 specification shows that the claimed exclusion criteria are mandatory outside of a clinical trial setting. *Id.* (citing Ex. 1107 ¶ 65).

With respect to the second part of the *Praxair* test, Petitioner contends that, even if the exclusion criteria were mandatory, they still would not be functionally related to the rest of the claims. Pet. Rely 11. Petitioner notes Patent Owner's argument that the exclusion criteria "define the patient population for treatment," but contends that the mental step of deciding not to treat a patient is unpatentable because "[o]nce the information is detected, no … treatment is given." *Id.* (quoting PO Resp. 23; Petition 26) (citation omitted).

Patent Owner responds that, with respect to Dr. Do's testimony, treating physicians can administer aflibercept in any number of ways, according to their medical judgment, but such administration will only practice the method of the challenged claims if it meets every claim limitation, including application of the exclusion criteria. PO Sur-Reply 8 (citing Ex. 2056 ¶ 158). Patent Owner adds that both parties' experts also agree that applying the exclusion criteria requires the active step of patient assessment to identify a treatment-eligible patient. *Id.* (citing Ex. 2323, 72–79).

Patent Owner argues again that the exclusion criteria define and limit the population of patients eligible for treatment. PO Sur-Reply 9. According to Patent Owner, to be eligible for the claimed treatment method, a patient must have an angiogenic eye disorder and must not have any of the recited excluded conditions. *Id.* Patent Owner contends that, by Petitioner's logic, no population-defining limitation for a method-of-treatment claim could be entitled to patentable weight, because patients who fall outside the defined population will not be treated as claimed. *Id.*

d. Analysis

We are persuaded by Petitioner's argument that the exclusion criteria are not limiting upon the claims. In *Praxair*, our reviewing court held that the printed matter doctrine is not limited to literal printed matter, but is also applicable when a claim limitation "claims the content of information" absent an adequate functional relationship. *Praxair*, 890 F.3d at 1032 (quoting *In re DiStefano*, 808 F.3d 845, 848 (Fed. Cir. 2015)). "Claim limitations directed to the content of information and lacking a requisite

functional relationship are not entitled to patentable weight because such information is not patent eligible subject matter under 35 U.S.C. § 101." *Id.* (citing *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1064 (Fed. Cir. 2010)).

If a claim limitation is directed to printed matter, the next step in the *Praxair* analysis is to determine whether the printed matter is functionally related to its "substrate." *Praxair*, 890 F.3d at 1032. Printed matter that is functionally related to its substrate is given patentable weight. *Id.* (citing *DiStefano*, 808 F.3d at 850). However, "[w]here the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability." *Id.* (quoting *In re Ngai*, 367 F.3d 1336, 1339 (Fed. Cir. 2004)).

More specifically, printed matter is functionally related to its substrate when the language changes not mere thoughts or outcomes, but provides action steps that the method requires. *See C R Bard Inc. v. AngioDynamics, Inc.*, 979 F.3d 1372, 1381 (Fed. Cir. 2020) (holding that the test for printed matter is whether it "merely informs people of the claimed information, or whether it instead interacts with the other elements of the claim to … cause a specific action in a claimed process."); *see also Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001) (stating that language "is only a statement of purpose and intended result" where its "expression *does not result in a manipulative difference in the steps of the claim*") (emphasis added).

In the case presently before us, there is little question that the exclusion criteria are directed to informational content. Specifically, the limitation in question expressly states that the "exclusion criteria for the

patient include all of: (1) active intraocular inflammation; (2) active ocular or periocular infection; (3) any ocular or periocular infection within the last 2 weeks." This list of conditions relays direct information to the practitioner of the claimed method as to the nature of the exclusion criteria, much in the manner of the listing of contraindications included with the packaging of any other drug. The exclusion criteria are certainly analogous to elements of claim 1 in *Praxair*, in which a practitioner of the claimed "method of providing pharmaceutically acceptable nitric oxide gas" provided information [to the medical provider]:

> [T]hat, in patients with preexisting left ventricular dysfunction, inhaled nitric oxide may increase pulmonary capillary wedge pressure (PCWP), leading to pulmonary edema, the information of (ii) being sufficient to cause a medical provider considering inhaled nitric oxide treatment for a plurality of neonatal patients who (a) are suffering from a condition for which inhaled nitric oxide is indicated, and (b) have pre-existing left ventricular dysfunction, to elect to avoid treating one or more of the plurality of patients with inhaled nitric oxide in order to avoid putting the one or more patients at risk of pulmonary edema.

Praxair, 890 F.3d at 1028–29. These limitations of claim 1 of *Praxair* (quoted above) and the exclusion criteria of the present challenged claims both provide information to the practitioner of the respective claimed methods concerning criteria to assess risks that may be incurred when practicing the method with a patient.

With respect to the second step of the *Praxair* analysis, however, we do not find that the exclusion criteria of the challenged claims are functionally related to the rest of the claim. The claims do not expressly recite any positive step to be performed (or a negative step *not* to be performed) should a patient meet the exclusion criteria. Patent Owner

attempts to distinguish the challenged claims from those of *Praxair* by arguing that the latter claims "were expressly directed to 'providing information' or a 'recommendation'" to the medical provider, which the medical provider was free to ignore. *See* PO Resp. 22. However, an individual practicing the method of the challenged claims would be similarly free to ignore the conditions of the exclusionary criteria and still be practicing the claimed method.

To be clear, and contrary to Patent Owner's argument, there are no positive or negative limitations in the challenged claims that *require* a person of ordinary skill in the art to act or not act in a certain way to practice the recited steps of the claimed method. As such, the information provided by the exclusionary criteria can be considered to be optional information, in that there is no direction to the practitioner to perform, or not perform, any specific step based upon the provided criteria. Thus, the exclusionary criteria are strictly informational, without requiring the practitioner to act, or refrain from acting, in a specified manner, and not functionally related to the practice of the claimed method.

Furthermore, *Rapoport* does not support Patent Owner's case. In *Rapoport*, an appeal from an interference proceeding before the Board, our reviewing court held that the Board was correct in interpreting "treatment of sleep apneas" as being limited to treatment of the underlying sleep apnea disorder, i.e., reducing the frequency and severity of the apnea episodes during sleep, and not additionally to treatment of anxiety secondary to sleep apnea. *Rapoport*, 254 F.3d at 1059–60. The court found that Board was correct in interpreting the language of the '681 Specification as distinctly limiting the construction of the disputed claim terms to the treatment only of

sleep apneas and not to secondary symptoms, such as anxiety. *Id.* Such is not the case in the present *inter partes* review. Patent Owner is not trying to expand the pool of eligible patients to include those with additional, related conditions, but argues that, by listing the exclusion criteria, the '681 patent is requiring the practitioner to actively exclude a set of patients. But, as we explain below, the language of the challenged claims does not support Patent Owner's arguments that the claims expressly or even implicitly *require* any action on the part of the practitioner based upon the exclusion criteria.

Patent Owner's reliance upon *Jansen* is similarly unavailing. The question before the Federal Circuit in *Jansen* was whether a preamble reciting "[a] method for treatment of sleep apneas comprising administration of a therapeutically effective amount of a Formula I azapirone compound or a pharmaceutically effective acid addition salt thereof to a patient in need of such treatment" was limiting upon the claim. *Jansen*, 342 F.3d at 1329, 1333–34. The court found that the preamble was limiting because it was "a statement of the intentional purpose for which the method must be performed." *Id.* The court did not find, as Patent Owner argues, that the preamble expressly limited the population of patients, or which patients should be excluded. *Id.*

In the present case, although the '681 Specification describes the use of the exclusion criteria in a clinical trial (Example 4), as we have explained, the exclusion criteria purportedly relate to the method of treatment, but propose no discrete manipulative difference in the steps by which the method, as practiced, should be altered by applying the exclusion criteria. *See Bristol-Myers*, 246 F.3d at 1376.

In the parallel district court proceedings, the district court, acknowledging our Institution Decision in the present *inter partes* review, arrived at the same conclusion with respect to essentially identical exclusion criteria limitations in Patent Owner's related '601 and '572 patents. Ex. 1112. Noting that the claim language, "wherein the exclusion criteria for the patient include" is written in the passive voice," the district court found that:

> The language does not require any action step to be taken as a consequence. Nothing has "transform[ed] the process of taking the drug" aflibercept in the claimed method—the "actual method" found in the underlying independent claim, e.g., 2 mg of aflibercept, on the stated dosing schedule, remains the same.

Id. at 34–35 (citing *King Pharms., Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1279 (Fed. Cir. 2010) (holding that when claim language did not change the underlying treatment method, it deserved no patentable weight).

The district court noted that, even under Patent Owner's "assess and exclude" approach, a patient either never starts the method (and hence the method doesn't change) or, if doctors screened for the information and found no infection or inflammation, the method proceeds as claimed. Ex. 1112, 35. The district court concluded that this confirms that the "exclusion criteria" are, at most, a non-binding informational "option" for doctors to consider. *Id.*

The Board made a similar point at oral argument concerning the same exclusion criteria in the related IPR2022-01226[14]:

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[14] Oral arguments in both the present *inter partes* review and IPR2022-01225 were heard sequentially and before the same panel on October 25, 2023. *See* Hearing Tr. 1.

> MS. DURIE: Well, I think you're right that it is flipped sides of the same coin, but I think it is important that what the exclusion criteria do is say, you do not have this condition. And therefore, you are eligible for treatment and the steps of the method may proceed.
>
> It is no different from any other criteria that is used to determine patient eligibility. And there is an entire body of case law that says determining that patients are eligible for treatment can be something that has patentable weight.
>
> ….
>
> JUDGE NEW: I would flip that around and say, wait a minute. The exclusion criteria say to a patient: you are not eligible for this treatment. We are not going to treat you. And therefore, the practice of the method is irrelevant.
>
> MS. DURIE: I think that argument could be used with any criteria that is used to determine patient eligibility. I would say it determines that a patient is eligible by saying, you have been screened. You do not have any of these conditions. You have not had active infection in the last two weeks. Therefore, the treatment may proceed.

Hearing Tr. 64.

In the district court proceedings, the court continued:

> Claims that had an actual active step based on the exclusion criteria to be analogous to the Praxair claim 9 situation would ***require*** that patients lacking ocular inflammation or infection participate in a modified method (such as a different drug, dose, or schedule); or ***require*** ongoing treatment to stop—but that would only happen if inflammation or infection arises while the method is underway, and [Patent Owner] insists its exclusion criteria are directed to pre-screening before the method even starts.

Ex. 1112, 35 (emphases in original). The court concluded that because "there is no requirement to take new action [or to take no action] that flows from the 'wherein the exclusion criteria for a patient include…' information, in a way that changes the existing treatment method, this claim language is construed to have no patentable weight." *Id.* at 37. We agree.

As the district court recognized, we are not bound by its decision (nor it by ours) because "the PTAB properly may reach a different conclusion based on the same evidence," for the Board and the district courts function under different evidentiary standards and burdens of proof. *See* Ex. 1112, 34 (citing *Novartis AG v. Noven Pharms. Inc.*, 853 F.3d 1289, 1293–94 (Fed. Cir. 2017). However, as the Federal Circuit recognized, "ideally" both district courts and the PTAB would reach the same results on the same record. *In re Baxter Int'l, Inc.*, 678 F.3d 1357, 1365 (Fed. Cir. 2012).

Such is the case in this instance. We find that the exclusion criteria recite informational content that does not result in a manipulative difference in the steps of the claim, and are therefore not functionally related to the claim. We consequently conclude that the exclusion criteria of the challenged claims are not entitled to patentable weight under the printed matter doctrine.

B. A Person of Ordinary Skill in the Art

Petitioner contends that a person of ordinary skill in the art would have: (1) knowledge regarding the diagnosis and treatment of angiogenic eye disorders, including the administration of therapies to treat said disorders; and (2) the ability to understand results and findings presented or published by others in the field. Pet. 28. Petitioner asserts that such a

person would typically have an advanced degree, such as an M.D. or Ph.D. (or equivalent, or less education but considerable professional experience in the medical, biotechnological, or pharmaceutical field), with practical academic or medical experience in (i) developing treatments for angiogenic eye disorders, including through the use of VEGF antagonists, or (ii) treating of same, including through the use of VEGF antagonists. *Id.* at 28–29 (citing Ex. 1002 ¶¶ 27–29; Ex. 1003 ¶¶ 21–25).

Patent Owner does not expressly contest this definition of a person of ordinary skill in the art in its Response. Because we find Petitioner's definition to be consistent with the level of skill in the art (*see, e.g.*, Exs. 1006, 1020), we adopt Petitioner's definition.

C. Ground 1: Anticipation under 35 U.S.C. § 102 of claims 1, 3–11, 13, 14, 16–24, and 26 by Dixon (Ex. 1006)

Claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent are challenged as unpatentable under 35 U.S.C. § 102 as being anticipated by Dixon. Pet. 48–52.

1. Overview of Dixon

Dixon was published in October, 2009, and is prior art to the '681 patent. Ex. 1006, 1573. Dixon discloses that a new drug for the treatment of age-related macular degeneration ("AMD") is aflibercept ("VEGF Trap-Eye"), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2. *Id.* Abstr. Dixon discloses that VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and II trial data indicating safety, tolerability and efficacy for the treatment of neovascular AMD. *Id.*

Dixon discloses that, structurally, VEGF Trap-Eye is a fusion protein consisting of key binding domains of human VEGFR-1 and -2 combined with a human IgG Fc fragment. Ex. 1006, 1575, Fig. 1. Dixon also discloses the PrONTO, CLEAR-IT-1, CLEAR-IT-2, and VIEW 1/VIEW 2 clinical trials. *Id.* at 1574–76, Ex. 1002 ¶ 74. Dixon identifies "[d]esirable attributes for emerging therapies for neovascular AMD include higher visual improvement rates and decreased dosing intervals" as a motivation for the "development of new drugs for neovascular AMD . . . focused on both improving efficacy and extending duration of action," Ex. 1006, 1574, 1577; Ex. 1002 ¶ 78.

Dixon further discloses results from the phase II clinical trial CLEAR-IT-2, which included four monthly doses (at weeks 0, 4, 8 and 12) followed by *pro re nata* ("PRN," "p.r.n.," or "prn") administration. Ex. 1006, 1576. Dixon reports that CLEAR-IT-2 subjects treated with that regimen exhibited mean improvement in visual acuity of nine letters and a mean decrease in retinal thickness of 143 μm. *Id.*; Ex. 1002 ¶¶ 79–80. Dixon further reports that "patients dosed at 2.0 mg during the initial monthly dosing period required 1.6 injections on average during the p.r.n. dosing phase." Ex. 1006, 1577. Dixon discloses that, in the CLEAR-IT-2 trial:

> Two groups received monthly doses of either 0.5 or 2.0 mg for 12 weeks (at weeks 0, 4, 8 and 12) and three groups received quarterly doses of either 0.5, 2.0 or 4.0 mg for 12 weeks (at weeks 0 and 12). Following this fixed dosing period, patients were treated with the same dose of VEGF Trap-Eye on a p.r.n. basis. Criteria for re-dosing included an increase in central retinal thickness of ≥ 100 μm by OCT, a loss of ≥ 5 ETDRS letters in conjunction with recurrent fluid by OCT, persistent fluid as indicated by OCT, new onset classic neovascularization, new or persistent leak on FA or new macular subretinal hemorrhage.

Id. at 1576. Dixon also discloses that "[p]atients initially treated with 2.0 or 0.5 mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p < 0.0001$) and 5.4 ($p < 0.085$) Early Treatment Diabetic Retinopathy Study ("ETDRS") letters with 29 and 19% gaining, respectively, ≥ 15 ETDRS letters at 52 weeks." *Id.*

Dixon also describes the then-ongoing VIEW 1/VIEW 2 phase III clinical trials. Ex. 1006, 1576. Dixon discloses that, with respect to the VIEW 1 trial:

> This non-inferiority study will evaluate the safety and efficacy of intravitreal VEGF Trap-Eye at doses of 0.5 and 2.0 mg administered at 4-week dosing intervals and 2.0 mg at an 8 week dosing interval (following three monthly doses), compared with 0.5 mg of ranibizumab administered every 4 weeks. After the first year of the study, patients will enter a second year of p.r.n. dosing evaluation. The VIEW 2 study has a similar study design.

Id. (internal citations omitted).

2. Challenged independent claims 1 and 14

In the -00881 Decision, we determined that independent claims 1 and 14 of the '338 patent were unpatentable under 35 U.S.C. § 102 as anticipated by Dixon. For the convenience of the reader, we present a claim chart comparing independent claim 1 of the present challenged claims and claim 1 of the '338 patent in the -00881 Decision:

IPR2022-01225 US 10,130,681 B2 Claim 1	**IPR2021-00881 US 9,254,338 B2 Claim 1 (unpatentable)**
1. A method for treating an angiogenic eye disorder in a patient,	1. A method for treating an angiogenic eye disorder in a patient,

said method comprising sequentially administering to the patient a single initial dose of a VEGF antagonist, followed by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;	said method comprising sequentially administering to the patient a single initial dose of a VEGF antagonist, followed by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;
wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;	wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2.	wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2.

wherein exclusion criteria for the patient include all of: (1) active intraocular inflammation; (2) active ocular or periocular infection; (3) any ocular or periocular infection within the last 2 weeks.	

As is evident from the chart above, challenged claim 1 of the present Petition and claim 1 of the '338 patent are identical, with the sole exception in the '681 patent of the additional limitation reciting the exclusion criteria. Similarly, challenged claim 14 of the present Petition and claim 14 of the '338 patent are identical, with the exception of the same exclusion criteria limitation added in the '681 patent.

Because, in the -00881 Decision, we concluded that claim 1 of the '338 patent is anticipated by Dixon, we incorporate here by reference our reasoning in the -00881 Decision with respect to the corresponding limitations of claim 1 of the '681 patent. *See* -00881 Decision, 26–46.

Briefly, in the -00881 Decision, we concluded that the preponderance of the evidence, including Dixon's express teaching that aflibercept and VEGF Trap-Eye have the "same molecular structure" demonstrated that Dixon inherently disclosed the claimed amino acid sequence of VEGF Trap-Eye (aflibercept). *See* Ex. 3001, 32–40. The Board found that the disclosures of Dixon, the prosecution history, and Patent Owner's own documents, demonstrated that aflibercept and VEGF Trap-Eye were the

same well-characterized single drug, rather than, as Patent Owner suggested, possibly a member of a vaguely defined genus of drugs, all called "VEGF Trap-Eye." *Id.* at 39.

Patent Owner makes essentially the same arguments in the present *inter partes* review (*see* PO Resp. 28–35) and, in view of the evidence of record, and our reasoning in the -00881 Decision, it fares no better than before. Of particular note is Patent Owner's argument that it's publications and Dixon, consistently refer to "VEGF Trap- Eye" as an ophthalmology drug and aflibercept as an oncology product. PO Resp. 35 (citing Ex. 2057 ¶¶ 39, 106–107; Ex. 2044, 101). Patent Owner points to Dr. Albini's testimony that it was "certainly possible" that a skilled artisan, reading Dixon could have concluded that VEGF Trap-Eye and aflibercept were different products. *Id.* (citing Ex. 2021, 342–343, 334–335). Patent Owner asserts that "this is fatal to Petitioner's inherency assertion." *Id.*

We disagree, and add that we addressed this issue extensively in the -00881 Decision. *See* Ex. 3001, 32–40. Dixon discloses that:

> VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure, but there are substantial differences between the preparation of the purified drug product and their formulations. Both aflibercept and VEGF Trap-Eye are manufactured in bioreactors from industry standard Chinese hamster ovary cells that overexpress the fusion protein. However, VEGF Trap-Eye undergoes further purification steps during manufacturing to minimize risk of irritation to the eye. VEGF Trap-Eye is also formulated with different buffers and at different concentrations (for buffers in common) suitable for the comfortable, non-irritating, direct injection into the eye.

Ex. 1006, 1575. Dixon thus teaches that the VEGF-antagonist, the active ingredient, in aflibercept and VEGF Trap-Eye are the same molecule (i.e., have the same molecular structure) but that the two medicaments are

thereafter formulated differently in that VEGF Trap undergoes further purification steps and uses different buffers appropriate for intraocular injection.

Furthermore, with respect to Dr. Albini's testimony as to whether a person of ordinary skill in the art "concluded that VEGF Trap-Eye and aflibercept were different products," Patent Owner mischaracterizes Dr. Albini's response:

> Q. Okay. Okay. So is it possible that the hypothetical person of ordinary skill in the art reading about a Phase 1 study of aflibercept, an oncology -- the oncology product in AMD and then separately a Phase 1 study of VEGF Trap-Eye in AMD may have reasonably concluded that these are different products?
>
> ….
>
> A. As I've already testified, I think it's certainly possible. But again, I think that a POSA would know that the molecule for treating eye disease that would be relevant to this patent would be the molecule in the CLEAR-IT-1 trial.

Ex. 2022, 342–343.

As Dr. Albini testifies, Dixon makes the distinction between the formulations containing the claimed VEGF receptor antagonist in terms of purification steps and buffers, but is clear on the point that the VEGF receptor antagonist in both formulations has the same molecular structure as that recited in the claims. *See also* Ex. 3001, 36–39 (concluding that Patent Owner's own documents demonstrate that VEGF Trap-Eye is its drug being used in the VIEW1 and VIEW 2 studies disclosed by Dixon).

Moreover, as Petitioner points out, Dixon also expressly discloses in its Abstract that "[o]ne promising new drug is aflibercept (VEGF Trap-Eye)," showing that persons of ordinary skill in the art knew VEGF Trap-

Eye and aflibercept, the molecular sequence of which was reported in the 2006 WHO index,[15] to refer to the same molecule as that recited in the challenged claims. (*See, e.g.*, Pet. 49; Ex. 1002 ¶¶ 83, 102, 152).

As we stated in the related IPR2021-00880, in which Patent Owner made the same arguments:

> Finally, as the above discussion and common sense strongly suggest, a drug that is reported in late Phase III clinical testing on human subjects is going to be a well-characterized single drug, rather than, as Patent Owner suggests, possibly a member of a vaguely defined genus of drugs, all called "VEGF Trap-Eye."

IPR2021-00880, Paper 89 at 58.

We incorporate by reference and adopt the reasoning of the -00881 Decision in the present case, and conclude that the preponderance of the evidence demonstrates that Dixon inherently discloses the "VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2," also known as aflibercept or VEGF Trap-Eye, as recited in challenged claims 1 and 4.

For the reasons explained in Section IV.A.3.d above, the exclusion criteria are entitled to no patentable weight. Because independent challenged claims 1 and 14 are otherwise identical to claims 1 and 14 of the '338 patent of the -00881 Decision, we conclude, for the same reasons set

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[15] "Aflibercept" in 20(2) WHO DRUG INFORMATION 118–19 (2006) (WHO index") (Ex. 1113).

forth in the -00881 Decision, that Petitioner has demonstrated, by a preponderance of the evidence, that challenged claims 1 and 14 of the '681 patent are unpatentable as being anticipated by Dixon.

3. Challenged dependent claims 3–11, 13, 16–24, and 26

Each of challenged claims 3–11, 13, 16–24, and 26 are identical to dependent claims 3–11, 13, 16–24, and 26 of the '338 patent, which were all found to be unpatentable as anticipated by Dixon in the -00881 Decision. *Compare* Ex. 1001, claims *with* IPR2021-00881, Ex. 1001, claims. Consequently, the only difference between these claims in the present *inter partes* review and the -00881 IPR is the incorporation of the exclusion criteria into the dependent claims from independent claims 1 or 14. *See Monsanto Co. v. Syngenta Seeds, Inc.*, 503 F.3d 1352, 1357 (Fed. Cir. 2007) (holding that "[a] claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers" (quoting 35 U.S.C § 112 ¶ 4 (2000))).

We have explained, in Section IV.A.3. above, why we conclude that the exclusion criteria are not accorded patentable weight. We therefore incorporate by reference and adopt the Board's reasoning and conclusions from the -00881 Decision with respect to the challenged claims in this *inter partes* review, and we conclude, for the same reasons, that Petitioner has shown, by a preponderance of the evidence, that dependent claims 3–11, 13, 16–24, and 26 of the '681 patent are anticipated by Dixon, and unpatentable. Furthermore, because we conclude that the challenged claims are unpatentable as anticipated by Dixon, we do not reach additional Grounds 2–6 of the Petition.

V. CONCLUSION

For the reasons we have explained, we conclude that Petitioner has demonstrated by a preponderance of the evidence, that challenged claims 1, 3–11, 13, 14, 16–24, and 26 of the '681 patent are unpatentable as being anticipated by Dixon. Furthermore, Petitioner's Motion to Exclude Evidence is granted-in-part, denied-in-part and dismissed-in-part. Patent Owner's Motion to Exclude Evidence is denied-in-part and dismissed-in-part.

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that based on a preponderance of the evidence, claims 1, 3–11, 13, 14, 16–24 and 26 of the '681 patent are unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude is granted in part, denied in part and dismissed in part; and

FURTHER ORDERED that Patent Owner's Motion to Exclude is denied in part and dismissed in part; and

FURTHER ORDERED that because this is a final written decision, the parties to this proceeding seeking judicial review of our Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

Claims	35 U.S.C. §	References	Claims Shown Unpatentable[16]	Claims Not shown Unpatentable
1, 3–11, 13, 14, 16–24, 26	102	Dixon	1, 3–11, 13, 14, 16–24, 26	
1, 3–11, 13, 14, 16–24, 26	102	Adis		
1, 3–11, 13, 14, 16–24, 26	102	Regeneron 2008		
1, 3–11, 13, 14, 16–24, 26	103	Dixon alone or in view of Papadopoulos and/or Wiegand		
1, 3–11, 13, 14, 16–24, 26	103	Dixon in combination with Rosenfeld-2006, and if necessary, Papadopoulos patent and/or Wiegand		
1, 3–11, 13, 14, 16–24, 26	103	Dixon in combination with Heimann-		

[16] As noted in Section III.A., we do not reach Petitioners' anticipation grounds based on Adis, Regeneron 2008, NCT-795, and NCT-377, or Petitioners' obviousness ground challenging claims 1, 3–11, 13, 14, 16–24 and 26 as we have determined that those claims are unpatentable based on the Dixon anticipation ground, as noted in the table.

		2007, and if necessary, Papadopoulos and/or Wiegand		
Overall Outcome			1, 3–11, 13, 14, 16–24, 26	

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