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Paper 101
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.

IPR2022-01226[1]
Patent 10,888,601 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 All Challenged Claims Unpatentable
35 U.S.C. § 318(a)

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[1] IPR2023-00533, *Celltrion, Inc. et al. v. Regeneron Pharms., Inc.*, and IPR2023-00566, *Samsung Bioepis Co., Ltd. v. Regeneron Pharms., Inc.*, have been joined with this *inter partes review*. *See* Papers 38, 39.

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 1–9, 34–39, 41–43, and 45 of Patent Owner Regeneron Pharmaceuticals, Inc.'s ("Patent Owner") U.S. Patent No. 10,888,601 B2 (Ex. 1001, the "'601 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 1–9, 34–39, 41–43, and 45 of the '601 patent. Patent Owner timely filed a Preliminary Response. (Paper 13, "Prelim. Resp."). With our authorization, Petitioner filed a Preliminary Reply and Patent Owner filed a Preliminary Sur-Reply. Paper 17 ("Prelim. Reply"); Paper 19 ("Prelim. Sur-Reply"). On January 1, 2022, and pursuant to 35 U.S.C. § 314, we instituted *inter partes* review. Paper 22 ("Institution Decision" or "Dec.").

After institution of trial, Patent Owner filed a Response (Paper 44, "PO Resp."), to which Petitioner filed a Reply (Paper 60, "Pet. Reply"), and Patent Owner, in turn, filed a Sur-Reply (Paper 65, "PO Sur-Reply").

Both Petitioner (Paper 76) and Patent Owner (Paper 77) filed Motions to Exclude Evidence ("Pet. Mot. Exclude" and "PO Mot. Exclude,"

respectively) and filed Oppositions (Papers 82 and 80) to the opposing party's Motion to Exclude Evidence (respectively, "Pet. Opp. Mot. Exclude" and "PO Opp. Mot. Exclude"). Both parties also filed a Reply to their opponent's Opposition to their Motions to Exclude ("Pet. Reply Mot. Exclude," "PO Reply Mot. Exclude").[2] Paper 83, Paper 84.

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 99 at 2. Patent Owner identifies Regeneron Pharmaceuticals, Inc. as the real party-in-interest. Paper 97 at 2.

B. Related Matters

Petitioner and Patent Owner identify *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-00880, IPR2021-00881, IPR2022-01225 (PTAB), and *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.), as related matters. Paper 5, 2; Paper 6, 1. Patent Owner also identifies *Chengdu Kanghong Biotechnology Co. v. Regeneron Pharms., Inc.*, PGR2021-00035 (PTAB) (proceeding terminated before

[2] Papers 44, 60, and 76 of the record are the unredacted versions of these papers. Papers 45, 59, 78 are the respective redacted versions of record.

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.*, 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 '601 patent, namely: US 9,254,338 B2; US 9,669,069 B2; US 10,857,205 B2; US 10,828,345 B2; US 10,130,681 B2; and 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 IPR2023-00533, *Celltrion, Inc. v. Regeneron Pharms. Inc.* and IPR2023-00566, *Samsung Bioepis Co., Ltd.*, both of which also challenged claims 1–9, 34–39, 41–43, and 45 of the '601 patent. *See* Papers 38, 39. Petitioners in the joined *inter partes* reviews acted as "silent understudies" in the present proceeding, and did not participate actively in the present proceeding. A copy of this Final Written Decision will be entered in each of IPR2023-00532 and IPR2023-00566.

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 '601 patent and US 9,254,338 B2 (the "'338 patent") at issue in IPR2021-00881 share a common specification. *Compare* Ex. 1001, *with* 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 1–9, 34–39, 41–43, and 45 of the '601 patent are unpatentable, based upon the following grounds:

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1	1–9, 34–39, 41–43, 45	102[3]	Dixon[4]
1	1–9, 34–39, 41–43, 45	102	Adis[5]
3	1–9, 34–39, 41–43, 45	102	Regeneron 2008[6]

[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 '601 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. 1007.

[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.

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
4	1–9, 34–39, 41–43, 45	102	NCT-795[7]
5	1–9, 34–39, 41–43, 45	103	Dixon alone or in view of Papadopoulos[8] and/or Wiegand[9]
6	1–9, 34–39, 41–43, 45	103	Dixon in combination with Rosenfeld-2006[10], and if necessary, Papadopoulos patent and/or Wiegand
7	1–9, 34–39, 41–43, 45	103	Dixon in combination with Heimann-2007, and if necessary, Papadopoulos and/or Wiegand

[7] ClinicalTrials.gov (archive), *Vascular Endothelial Growth Factor (VEGF)Trap-Eye: Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (AMD) (VIEW1)*, *available at*: https://clinicaltrials.gov/ct2/history/NCT00509795?A=8&B=9&C=merged#StudyPageTop (last visited December 21, 2022) Ex. 1014.

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

[9] Wiegand et al. (US 7,531,173 B2, May 12, 2009) ("Wiegand") Ex. 1008.

[10] 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.

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 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 '601 Patent

The '601 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, cols. 2–3, ll. 63–2.

E. Representative Claim

Independent claim 34 is representative of the challenged claims, and recites:

> 34. A method for treating an angiogenic eye disorder in a patient in need thereof, said method comprising administering to the patient an effective sequential dosing regimen of 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 4 weeks after the immediately preceding dose; and
>
> wherein the VEGF antagonist is a receptor-based chimeric molecule comprising an immunoglobin-like (Ig) domain 2 of a first VEGF receptor which is VEGFR1 and an Ig domain 3 of a second VEGF receptor which is VEGFR2, and a multimerizing component
>
> wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
>
> wherein the VEGF antagonist is a receptor-based chimeric molecule comprising an immunoglobin-like (Ig) domain 2 of a first VEGF receptor which is VEGFR1 and an Ig domain 3 of a second VEGF receptor which is VEGFR2, and a multimerizing component.

Ex. 1001, col. 24, ll. 4–19.[11]

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[11] 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,

F. Priority History of the '601 Patent

The '601 patent issued from U.S. Application Ser. No. 16/397,267 (the "'267 application") filed on April 29, 2019, and claims the priority 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 '601 patent, including challenged claims 1–9, 34–39, 41–43, and 45 were allowed on November 12, 2020, and the patent issued on January 12, 2021. Ex. 1017, 5591; 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 Motions 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, 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.

1575 ("VEGF Trap-Eye and aflibercept … have the same molecular structure").

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, 108–09, 113–16, and attachments C1–C12, D1–D4, D7, and X2)

Petitioner argues that Patent Owner relies on the testimony of its expert, Dr. Manning, in support of its commercial success contentions. Pet. Mot. Exclude 1–2 (citing, e.g., PO Resp. 2, 41, 56–57; 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, 108–109, 113–116. *Id.* Petitioner states that it timely objected to the challenged Financial Exhibits. *Id.* (citing Papers 24, 49).

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). Pet. Mot. Exclude 2–5.

As Petitioner states, Patent Owner relies upon these Exhibits as objective secondary evidence of non-obviousness. *See, e.g.*, PO Resp. 55–57. 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 5–7) or its contentions regarding secondary considerations of non-obviousness. *See Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1364 (Fed. Cor. 2008) (holding that "secondary considerations are not an element of a claim of anticipation"). Consequently, we dismiss Petitioner's motion to exclude 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 secondary objective indicia of no-obviousness. Petitioner states that it timely objected to the challenged Marketing Exhibits. *Id.* (citing Papers 24, 49).

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 5–7), 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 VEGFR2 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 '601 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.*

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 '601 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 that 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 '601 patent. 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 '601 patent. The same is true for Exhibits 2084 and 2085 with respect to VEGFR2 (accession no. P35968). Petitioner does not contest that the database was publicly available, and we conclude that the Exhibits are 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, 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 9 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[12] 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. 1999) (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 a person of ordinary skill's

[12] 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 IPR2022-01225, which was argued at the same item as the present *inter partes* review.

knowledge or a prior art teaching. *Id.* Petitioner contends that any probative value of the 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 or Exhibit 2049 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 1342. In the absence of any such authentication, we consequently grant Petitioner's motion to exclude Exhibit 2122 as impermissible hearsay under FRE 803.

d. 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 401–402. Pet. Mot. Exclude 12. 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 12–13. 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.

e. 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 13–14 (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, 120–121, 123–128), Dr. Brown (Ex. 2055 ¶ 67), and Dr. Manning (Ex. 2059 ¶¶ 11, 28–29, 43, 47–117). *Id.* at 14.

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 13. Patent Owner contends that Petitioner's assertions lack particularity and do not satisfy Petitioner's burden on a motion to exclude. *Id.* at 13–14.

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 14 (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. Ex. 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, 2228, and 2229. We similarly deny Petitioner's motion to exclude the portions of Patent Owner's experts' 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, 1009, 1015, 1020, 1087, 1108, 1167, 1124, 1150, and 1151 and related portions of Exhibits 1002, 1003, 1107, and 1115. PO Mot. Exclude 1, 10. We consider each of Patent Owner's arguments in turn.

1. Ex. 1058

Patent Owner argues that Exhibit 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 being obvious over the cited prior art. *See* Pet. 12.

Patent Owner argues that Exhibit 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.

2. Exhibits 1009, 1015, 1020, 1087, 1108, 1167, and related portions of Exhibits 1002, 1003, 1107, and 1115

Patent Owner next urges us to exclude Exhibits 1009, 1015, 1020, 1087, 1108, and 1167 on the basis that none of these Exhibits were cited in the Petition or the Petitioner's Reply. PO Mot. Exclude 9. Similarly, Patent Owner seeks to exclude the related portions of Petitioner's expert testimony not cited in the pleadings:

(i) Ex. 1002 ¶¶ 30–47, 53–63, 65–68, 70–71, 75–82, 87–92, 98–99, 112, 114, 119, 121, 123, 130–133, 138–140, 142, 161, 164–66, 170–171, 173–174, 177–178, 180, 209–215, 225, 249–255, 285–291, 344–345, and 352–353;

(ii) Ex. 1003 ¶¶ 31–41;

(iii) Ex. 1107 ¶¶ 6–64, 66–71, 79–86, 92–93, 101, and 102–127;

(iv) Ex. 1115 ¶¶ 28–59.

Id. at 10, 15. 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.*

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 1009, 1015, 1020, 1087, 1108, and 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*, IPR2019-01649, Paper 43, 32–33. 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 1009, 1015, 1020, 1087, 1108, and 1167, and the challenged paragraphs of Exhibits 1102, 1103, 1107, and 1115.

3. 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 11–14.

Dr. Manning's testimony relates to the commercial success of the compound recited in the challenged claims as secondary 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 5–7. We therefore do not rely upon Dr. Manning's testimony as to objective indicia of nonobviousness. Nor does our analysis rely upon, or cite to, the Exhibits challenged by Patent Owner. *Cohesive Techs.*, 543 F.3d at 1364. Consequently, we dismiss as moot Patent Owner's motion to exclude Exhibits 1124, 1150, and 1151.

f. 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 1009, 1015, 1020, 1087, 1108, and 1167, and the related portions of Exhibits 1002, 1003, 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. 15–22. Petitioner also argues that the limitation reciting "wherein exclusion criteria for the patient include all of…." (the "exclusion criteria") of claims 9 and 36 are not entitled to patentable weight under the printed matter doctrine. *Id.* at 23–25. Petitioner, it its Reply Brief, further argues that the limitations of claims 5 and 6 establishing Best Corrected Visual Acuity ("BCVA") performance criteria also lack patentable weight. Pet. Reply 11–12. Finally, Petitioner additionally proposes constructions for the claim terms "initial dose," "secondary dose," and "tertiary dose." Pet. 22–23.

Patent Owner argues that: (1) the challenged claims require effective treatment; and (2) the exclusion criteria recited in challenged claims 9 and 36 are limiting upon the claims. PO Resp. 8–23. Patent Owner also challenges Petitioner contention that the limitations establishing BCVA criteria lack patentable weight. PO Sur-Reply 10–13.

On October 27, 2023, subsequent to oral argument, the Board authorized additional briefing by the parties on their proposed claim construction of the claim term "effective sequential dosing regimen," as recited in challenged claim 34. Both parties filed their proposed constructions ("Pet. CC" and "PO CC", Papers 94, 93) and Oppositions to the opposing party's construction ("Pet. CC Opp." and "PO CC Opp.", Papers 95, 96).

We address each of the parties' arguments in turn.

1. Construction of "effective amount" in the preambles of claims 1 and 10 and "effective sequential dosing regimen" in the preamble of claim 34)

a. Petitioner's arguments

Petitioner argues the preamble is not limiting upon the claims. Pet. 15–16. 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. *Id.* at 15–16, 18. 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 18–22.

b. Patent Owner's Response

Patent Owner acknowledges the Board's finding in its Institution Decision that the preamble of the challenged claims require "treating an angiogenic eye disorder in a patient." PO Resp. 9–10 (citing Dec. 10; also citing Ex. 2056 ¶ 81). Patent Owner contends that the challenged claims further require that the "method for treating" actually be effective, asserting

that challenged claims 1, 2 and 5–9 expressly state that the claimed method requires administering an "effective amount of aflibercept which is 2 mg" for the treatment of wet AMD. *Id.* at 10 (citing Ex. 1001, col. 21, ll. 43–44, 47–48, 55–67; Ex. 2056 ¶¶ 83, 85). Patent Owner asserts that claims 34–39, 41–43, and 45 of the '601 patent similarly state that the claimed method requires administering an "effective sequential dosing regimen" for treatment of an angiogenic eye disorder. *Id.* (citing Ex. 1001, col. 24, ll. 6, 20–32, 35–43, 46–47); Ex. 2056 ¶¶ 84–85).

Patent Owner points to the Board's Final Written Decision in the related -00881 IPR, in which the Board recognized that including efficacy language, e.g., "effective amount," in the body of the claims signals that the method must actually be effective (i.e., result in a beneficial effect) in a given patient. PO Resp. 10 (citing Ex. 3001, 20). According to Patent Owner, the language "effective sequential dosing regimen" in claim 34 and its dependents signals the same. *Id.* at 10–11. Patent Owner therefore asserts that, contrary to Petitioner's assertion, administration of aflibercept in the claimed doses and frequency is not sufficient to practice the claimed method. *Id.* at 11. Rather, argues Patent Owner, the challenged claims expressly require that the patient receive effective treatment. *Id.* (citing Pet. 61 n.10; Ex. 2056 ¶¶ 82–85).

Patent Owner asserts that the '601 Specification confirms that effective treatment of an angiogenic eye disorder is the essence of the claimed invention. PO Resp. 11 (citing Ex. 1001, col. 1, ll. 25–27, also citing *id.* at col. 2, ll. 3–5, 29–30, col. 7, ll. 27–30). Patent Owner notes that the '601 Specification also discloses that the inventor "surprisingly discovered that beneficial therapeutic effects can be achieved" with the

claimed method. *Id.* (quoting Ex. 1001, col. 2, ll. 11–17; also citing Ex. 2056 ¶¶ 86–87). Patent Owner argues that a critical aspect of the invention is efficacy is further confirmed by the Specification's disclosure that there was a need in the art for "efficac[ious]" extended dosing regimens, immediately following the Specification's reference to a prior unsuccessful trial in which extended dosing of Lucentis was not effective. *Id.* (citing Ex. 1001, col. 1, ll. 61–67; Ex. 2024). Patent Owner therefore argues that a person of ordinary skill in the art, reading the claims recital of "effective" treatment, in view of the Specification, would understand the claims to require such effective treatment. *Id.* at 12 (citing Ex. 2056 ¶¶ 81–87).[13]

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

Petitioner replies that Patent Owner's proposed "effectively treating" construction would require, as concluded by the -00881 Decision, "improperly importing limitations into the claims." Pet. Reply 3 (quoting Ex. 3001, 22). Petitioner contends that Patent Owner does not dispute that efficacy is not literally written in the claims. *Id.* Petitioner points out that the '601 Specification nowhere defines or guides how a skilled artisan should ascertain, measure, or differentiate "effectively treating." *Id.* Nor, argues Petitioner, does Patent Owner proffer an actual construction in its Response. *Id.*

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[13] Patent Owner also rebuts Petitioner's allegations that Patent Owner's proposed construction poses "enablement, written description, and definiteness problems" for the challenged claims. PO Resp. 12–15. We need not reach either Petitioner's or Patent Owner's response in this respect to arrive at an appropriate claim construction.

Petitioner responds that, in the -00881 Decision, the Board recognized that "including efficacy language, e.g., 'effective amount,' in the body of the claims…signals that the method must actually be effective." Pet. Reply 3 (citing Ex. 3001, 20) (alteration in original). However, Petitioner notes, the Board made clear that it was not suggesting "any categorical rule regarding a requirement for therapeutic effectiveness based upon the inclusion or omission of that claim phrase alone." *Id.* (quoting Ex. 3001, 20 n.11).

Petitioner contends that, during prosecution of the '601 patent, Patent Owner and its experts proposed claim construction of "effectively treating" as meaning "noninferior," "statistically noninferior," or "comparable." Pet. Reply 4. Petitioner asserts that Patent Owner, and its expert, Dr. Do, advance the proposed construction of "effectively treating, " with no explanation for what that means, or how it comports with the challenged dependent claims that recite visual acuity limitations ranging from losing less than 15 letters to gaining more than 15 letters. *Id.* at 4–5.

Petitioner also argues that Patent Owner's two experts, Dr. Do and Dr. Brown, offer contradictory testimony as to which patients received the claimed method of treatment: Dr. Do testified that "the 5.6 percent of patients who lost 15 or more letters on the 2Q8 arm, they did not practice the claimed method of treatment because they did not achieve and maintain a high level of efficacy comparable to that seen with Lucentis [i.e., ranibizumab]." Pet. Reply 5 (quoting Ex. 1109, 97) (alteration in original). But, argues Petitioner, Dr. Brown, when asked whether patients in the VEGF Trap-Eye 8-week dosing arm received treatment that was "non-inferior to ranibizumab," testified that "everyone in the cohort met non-inferiority." *Id.* (citing Ex. 1110, 52).

Petitioner asserts that Dr. Do's opinion that "effective" treatment means "far more than the mere loss of 15 or fewer letters" also contradicts the intrinsic record. Pet. Reply 5 (quoting Ex. 2056 ¶ 79). Petitioner points out that challenged dependent claim 3 recites a method for treating "wherein the patient loses less than 15 letters of Best Corrected Visual Acuity (BCVA) score." *Id.* (citing Ex. 1001, claim 3). Petitioner argues that the scope of Claim 1 must therefore include cases "wherein the patient loses less than 15 letters" as "effective treatment." *Id.* at 6. Petitioner contends that the Board should discount Dr. Do's testimony because it "is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history." *Id.* (quoting *Phillips*, 415 F.3d at 1318; and citing (Ex. 1107 ¶¶ 11–30, 45–48).

Patent Owner responds that, contrary to Petitioner's position, the preamble is limiting and requires efficacy. PO Sur-Reply 2. Patent Owner asserts that every challenged claim expressly requires effective treatment and thus disputes Petitioner's assertion that "efficacy is not literally written in the claims." *Id.* (quoting Pet. Reply 3). According to Patent Owner, the evidence of record shows that, as of 2011, a skilled artisan would have understood "effective treatment" to mean treatment comparable to or on par with standard-of-care, i.e., monthly Lucentis or Avastin. *Id.* at 2 (citing PO Resp. 11–12).

Patent Owner points to Petitioner's expert, Dr. Albini's testimony that his pre-2011 treatment goal for patients with angiogenic eye disorders was aligned with PO's construction:

> Q: [W]ithin a given patient, you would hope that your PRN [as-needed] dosing of that patient got them efficacy that

> was as good as they personally would get with monthly dosing of Lucentis; is that right?
>
> A: That's correct.

PO Sur-Reply 3 (quoting Ex. 2347, 127) (alterations in original). Patent Owner contends that this meant visual acuity gains, not losses, and not merely achieving the clinical trial endpoint of loss of ≤ 15 letters on ETDRS. *Id.* (citing PO Resp. 3–4; Ex. 2056 ¶¶ 78–79). Patent Owner therefore asserts that its construction does not require "importing limitations into the claims." *Id.* at 4.

Patent Owner accuses Petitioner of ignoring the claim term "effective," rather than proposing a claim term for it. PO Sur-Reply 4 (citing Pet. Reply 2–3). Patent Owner contends that Petitioner's reliance upon the Board's claim construction ruling in IPR2021-00881 similarly disregards the differences between the language of the respective claims. *Id.* (citing, e.g., *Wasica Fin. GmbH v. Cont'l Auto. Sys., Inc.*, 853 F.3d 1272, 1288 n.10 (Fed. Cir. 2017) ("holding that "[i]t is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous")).

Patent Owner also disputes Petitioner's contention that Patent Owner's construction is "contradictory". PO Sur-Reply 4 (citing Pet. Reply 3–5). Patent Owner contends that Petitioner conflates expert testimony concerning randomized clinical trials conducted on a population basis (and their population-based outcome measures) with testimony concerning treatment of individual patients. *Id.* at 4–5. Patent Owner argues that it is undisputed between the parties that the challenged claims are directed to treating "a patient." *Id.* at 5 (citing Ex. 1107 ¶ 40) (emphasis omitted). According to Patent Owner, both parties' experts agree that a person of

ordinary skill in the art would not use statistical non-inferiority or clinical-trial-based outcome measures when assessing individual-patient efficacy. *Id.* (citing Ex. 2347, 127). Patent Owner also contends that both parties' experts agree that those of ordinary skill in the art would have understood effective treatment to mean treatment on par with monthly administration of Lucentis (or Avastin). *Id.* (citing Ex. 2347, 127).

Patent Owner argues further that its expert, Dr. Do, explained that the colloquial use of the term "non-inferior" in connection with an individual patient means "comparable to," or "on par with" treatment with monthly Lucentis or Avastin. PO Sur-Reply 5 (citing Ex. 1109, 15–16, 22–24, 24–30, 34, 42; Ex. 2056 ¶ 78). Patent Owner notes that Dr. Brown agreed with Dr. Do's construction, and also agreed that one does not measure statistical non-inferiority when treating an individual patient. *Id.* at 5–6 (citing Ex. 2055 ¶¶ 104–105; Ex. 1110, 50). Patent Owner also notes that Dr. Albini also agreed that clinicians using anti-VEGF agents pre-2011 sought efficacy "as good as" what the patient would achieve with monthly Lucentis. *Id.* at 6 (citing Ex. 2347, 127).

Patent Owner argues that its construction is consistent with the intrinsic record. PO Sur-Reply 6. According to Patent Owner, Petitioner quotes from the prosecution history of the '601 patent, but omits that Patent Owner highlighted vision gains achieved with Q8 dosing. *Id.* (citing Pet. Reply 4; Ex. 2331, 290).

d. Related argument regarding "administering to the patient an effective sequential dosing regimen"

Relatedly, and subsequent to hearing oral argument in this *inter partes* review, the Board invited the parties to submit additional briefing upon their proposed construction of the claim term "effective sequential dosing regimen," as recited in challenged claim 34. Paper 91. As authorized, both parties submitted briefs (respectively "Pet. CC" (Paper 94) and "PO CC" (Paper 93)) as well as Oppositions to the opposing party's brief (respectively "Pet. CC Opp." (Paper 95) and "PO CC Opp." (Paper 96)). We now turn to these arguments.

e. Petitioner's and Patent Owner's claim constructions

Petitioner points to its Petition, which states that claim 34 defines "an effective sequential dosing regimen as [the regimen] having the recited steps." Pet. CC 1 (citing Pet. 53 n.8, 61 n.10) (alteration in original). Petitioner argues that the steps follow the framework of "a single initial dose … followed by one or more secondary doses … followed by one or more tertiary doses," and that the '601 Specification ties this regimen to efficacy. *Id.* (alterations in original). Petitioner asserts that Patent Owner's proposed construction improperly relies on extrinsic evidence to rewrite claim 34 as requiring "effective treatment" to import a "standard-of-care, *i.e.,* monthly Lucentis or Avastin" claim meaning, which contradicts the intrinsic evidence. *Id.* (citing PO Resp. 3; Ex. 1002 ¶¶ 52, 153).

Petitioner points to the testimony of Dr. Albini, who opined that "no particular level of efficacy is required by any of the covered methods for treating." Pet. CC 1 (quoting Ex. 1107 ¶ 13). Rather, stated Dr. Albini, the goal is "inhibiting the angiogenic-promoting properties of VEGF." *Id.* at 1–

2 (citing Ex. 1107 ¶ 109). Petitioner notes that the '601 Specification calls this "an effective strategy for treating angiogenic eye disorders," discloses a wide range of clinical outcomes. *Id.* at 2 (quoting Ex. 1001, col. 1, ll. 54–56, Table 1, Table 2; also citing Ex. 1018, 2542).

Petitioner argues that, just as challenged claim 1 recites administering with an "effective amount" of the drug, defining the dose with the phrase "which is," claim 34 recites an "effective sequential dosing regimen of" drug doses, defining that regimen by what follows after "of." Pet. CC 2 (quoting Ex. 1001, claim 1, claim 34). According to Petitioner, challenged claim 34's dependent claims confirm that the manipulative steps in the "effective" regimen sequence framework (initial, secondary, tertiary) never change based on clinical outcomes or standards. *Id.* Rather, argues Petitioner, those claims narrowly define the types of doses administered. *Id.* (citing Ex. 1001, claim 35, claim 38, claim 41).

Petitioner points to Dr. Do's testimony to illustrate why an "effective … regimen" requires only this framework. Pet. CC 2. Petitioner states that when Dr. Do applied the "effective sequential dosing regimen" to claim that Eylea satisfied this element, she offered no proof of clinical performance—only the existence of the regimen steps. *Id.* (citing Ex. 2056 ¶ 135). Petitioner asserts that neither Dr. Do nor Dr. Brown could consistently delineate how or when a patient was in an "ineffective" regimen versus one with a "high level of efficacy," that was noninferior to the "standard of care," which was "Lucentis or Avastin," which undermines Patent Owner's proposed construction. *Id.* at 2–3 (citing Ex. 1109, 104–110, 121–126; Ex. 1110, 39; Ex. 2036, 81).

Petitioner contends that the '601 Specification states that the alleged need that the "present invention" purportedly solved was the regimen. Pet. CC 3 (citing Ex. 1001, col. 1, ll. 64–67 ("there remains a need in the art for new administration regimens for angiogenic eye disorders, especially those which allow for less frequent dosing while maintaining a high level of efficacy"); also citing *id.* at col. 1, ll. 64–67; col. 4, ll. 48–50, col. 3, ll. 30–41, col. 2, ll. 1–31, col. 3, ll. 42–44). Petitioner argues that, in define a "therapeutically effective" amount, the Specification broadly included doses that produced any "detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder," or "inhibits, prevents, lessens, or delays the progression of an angiogenic eye disorder." *Id.* at 3–4 (citing Ex. 1001, col. 6, ll. 60–65).

Petitioner contends that the '601 Specification's more general discussion of efficacy also does not impose thresholds on par with Lucentis or Avastin, or employs the phrase "standard of care." Pet. CC 4 (citing Ex. 1001, col. 7, ll. 26–43). Rather, the Specification discloses that "[g]enerally, the methods of the present invention demonstrate efficacy within 104 weeks of the initiation of the treatment regimen," with "efficacy" arising when, "from the initiation of treatment, the patient exhibits a loss of 15 or fewer letters on the" ETDRS visual acuity chart. *Id.* (citing Ex. 1001, col. 7, ll. 30–40). Petitioner also notes that the Specification describes gains of one or more letters from initiating treatment as "embodiments" of the invention. *Id.* (citing Ex. 1001, col. 7, ll. 40–43).

Petitioner argues that none of these outcomes or benefits measured according to metrics found in the Examples warrant exclusion from the meaning of an "effective … regimen," or even Patent Owner's "effective

treatment" alternative. Pet. CC 4. Petitioner contends that this is especially so when, as Dr. Albini explained, the Specification proposes that "'beneficial therapeutic effects can be achieved in patients suffering from angiogenic eye disorders by administering a VEGF antagonist,' and not that such effects must be achieved." *Id.* (citing Ex. 1002 ¶ 48 (quoting Ex. 1001, col. 2, ll. 11–17)).

Petitioner notes that Patent Owner relies upon Example 4 and the Specification's "high level of efficacy" language to try to justify importing its standard-of-care meaning. Pet. CC 4. Petitioner asserts that the latter phrase appears after "especially those…," signaling that high efficacy is a desirable embodiment, not the entire invention. *Id.* at 4–5 (citing Ex. 1001, col. 1, ll. 64–67). However, argues Petitioner, the Specification expressly warns that the claims' scope is limited "only by the appended claims," not the embodiments disclosed. *Id.* at 5 (quoting Ex. 1001, col. 3, ll. 9–13).

Finally, Petitioner argues that, during prosecution of this patent family, Patent Owner called Heier-2012's[14] results "unexpected." Pet. CC 5 (citing PO Resp. 55 n.21 (citing Ex. 2331, 288–91)). According to Petitioner, Heier-2012's primary efficacy metric was the comparative percentage of patients losing < 15 letters compared to ranibizumab, which Dr. Do allegedly insisted is not the standard of care. *Id.* (citing Ex. 1018, 2542; Ex. 2056 ¶¶ 64, 69, 79). Petitioner contends that Patent Owner's construction thus excludes an embodiment the Specification calls "efficac[ious]." *Id.* (citing Ex. 1001, col. 7, ll. 36–40).

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[14] J.S. Heier, *Intravitreal Aflibercept (VEGF Trap-Eye) in Wet Age-related Macular Degeneration*, 119(12) OPHTHALMOL. 2537–48 (2012) ("Heier-2012") Ex. 1018.

Patent Owner responds that Petitioner's proposed construction invites error by asking the Board to ignore an express claim term. PO CC Opp. 1. Patent Owner contends that an "effective sequential dosing regimen" requires efficacy, and that to find otherwise would distort claim 34 to encompass sequential administration of minute doses of VEGF antagonist—resulting in a regimen that no one of skill in the art would deem "effective." *Id.* Patent Owner argues that the weight of the evidence of record shows that a person of ordinary skill in the art would only view the "effective sequential dosing regimen" of the '601 patent as effective if it maintained the treatment efficacy reflected in the standard-of-care, i.e., monthly Lucentis. *Id.* (citing PO Resp. 3–6, 41–43; PO Sur-Reply 2–6).

Patent Owner again contends that Petitioner's proposed construction renders an express claim term meaningless. For example, if the "effective sequential dosing regimen" requires nothing but sequential dosing, challenged claim 34 would encompass administering infinitesimal quantities of VEGF antagonist, incapable of achieving any treatment efficacy. PO CC Opp. 2. Patent Owner contends that both parties' experts agree that a person of ordinary skill in the art would not understand the '601 Specification's reference to "efficacy" to provide a clear definition for the claimed methods for treating. *Id.* (citing Ex. 2021, 177–181; Ex. 2056 ¶¶ 66, 78–79). Patent Owner contends that it is undisputed that no one portion of the Specification defines this phrase, and it must therefore be interpreted in context and given the meaning that a skilled artisan would have ascribed to it in 2011. *Id.* at 2–3 (citing, e.g., *Aventis Pharms. Inc. v. Amino Chems. Ltd.*, 715 F.3d 1363, 1373–74 (Fed. Cir. 2013)).

Patent Owner argues that although Petitioner points to various passages from the '601 Specification, it fails to provide any proposed construction or evidence for how a person of ordinary skill in the art would have understood the intrinsic record to inform the recited "effective sequential dosing regimen" limitation. PO CC Opp. 3. According to Patent Owner, the testimony of both parties' experts testimony supports Patent Owner' contention that a skilled artisan would have expected the "effective sequential dosing regimen" to provide efficacy on par with standard-of-care treatment, i.e., monthly Lucentis. *Id.* at 4 (citing PO Resp. 3–4, 41, 43; PO Sur-Reply 3–4; Ex. 2347, 127). Conversely, argues Patent Owner, no person of ordinary skill in the art would have viewed an extended dosing regimen that was inferior to the standard-of-care as "effective" for treating angiogenic eye disorders. *Id.* (citing PO Resp. 41–43; PO Sur-Reply 2–6).

Finally, Patent Owner argues that to the extent that the Board finds that the challenged claims require some non-zero level of efficacy other than that advanced by Patent Owner, it will be a new construction, neither advocated nor addressed by either party, and consequentially prejudicial to Patent Owner. PO CC Opp. 5. Patent Owner makes essentially the same arguments in its proposed claim construction brief that it does in its Response and Sur-Reply. *See* PO CC 1–5.

f. Analysis

We addressed similar arguments in the prior -00881 Decision. *See* Ex. 3001, 12–23. The difference in this case is that the challenged claims of the '601 patent recite the claim term "effective" in its preamble, e.g., "intravitreally administering, to said patient, an effective amount of

aflibercept" (claim 1, claim 10, claim 18); and "administering to the patient an effective sequential dosing regimen of a single initial dose of a VEGF antagonist…." (claim 34).

Petitioner contends that the preamble is not limiting upon the claims, but if it is limiting, the language of the claims is such that "no particular level of efficacy is required by any of the covered methods for treating," but rather that the goal of the invention is "inhibiting the angiogenic-promoting properties of VEGF." *See* Pet. 15–16, 18; Pet. CC 1 (quoting Ex. 1107 ¶¶ 13, 109). Patent Owner contends that the use of the claim term "effective" requires that the administered doses of the VEGF receptor antagonist demonstrate a high level of efficacy, one that is comparable to that achieved by monthly doses of certain other VEGF receptor antagonists, i.e., Lucentis and off-label Avastin. *See, e.g.*, PO Resp. 11–13, 41–43.

As an initial matter, we have previously addressed whether the preamble is limiting upon the claims in, *inter alia*, the -00881 Decision. In that Decision, we explained that:

> [T]he 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." *See* Claims 1 and 14, Ex. 1001, 23:2–3; 24:3–4. The Specification repeatedly characterizes the method as one for treating angiogenic eye disorders in patients. *See, e.g., id.* at 1:18–20, 63–66, 2:23–27; 3:19–20; 5:11–13. 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.

Ex. 3001, 17–18. We concluded that:

> [I]n view of Federal Circuit case law regarding statements of intended purpose in claims directed to method of using compositions, and 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 18. The similar language of the challenged claims of the '601 patent, and our reasoning in the related -00881 Decision, compel the same conclusion here, i.e., that the preamble is limiting upon the claims.

We also addressed in the -00881 Decision whether the claims required, as Patent Owner argued, any degree of efficacy. Then, as now, Patent Owner argued that "treating" an angiogenic eye disorder requires achieving "a high level of efficacy, on par with the prevailing standard-of-care at the time of filing." Ex. 3001, 19 (quoting IPR2021-00881, Paper 41 at 13 (PO Resp.)). In our -00881 Decision, we reasoned that:

> [W]e find instructive the Specification's discussion [which is identical to that of the '601 patent] regarding the "Amount of VEGF Antagonist Administered." In that discussion, the Specification explains,
>
> > The amount of VEGF antagonist administered to the patient in each dose is, *in most cases*, a therapeutically effective amount. As used herein, the phrase "therapeutically effective amount" means a dose of VEGF antagonist that results in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or a dose of VEGF antagonist that inhibits, prevents, lessens or delays the progression of an angiogenic eye disorder.
>
> (emphasis added). That description, along with the absence of the phrase "therapeutically effective" in the claims,11 signals for us the inventors' intention to not limit the claims to the

> administration of doses that ultimately prove to be therapeutically effective in a given patient. Instead, the Specification describes administration of VEGF antagonist doses for treating angiogenic eye disorder in a manner that encompasses doses that result in disclosed improvements and benefits, referred to as "therapeutically effective amounts," and doses that do not. Indeed, as guidance, the Specification discloses that "a therapeutically effective amount *can* be from about 0.05 mg to about 5 mg," without any guarantee that any particular dosage regimen administered within that range of dosage amounts will necessarily be "therapeutically effective," and without limiting the treatment methods based upon such results.

Ex. 3001, 20 (citations omitted, emphases added).

However, in the present *inter partes* review, the challenged claims *do* recite that the dose administered should be an "effective amount" (claims 1 and 10) or "an effective sequential dosing regimen" (claim 34). The question squarely presented, then, is whether the use of the claim term "effective," which is not present in the challenged claims of the -00881 IPR, requires, as Patent Owner contends, a "high level of efficacy" comparable to that of Lucentis or off-label Avastin. *See* PO Resp. 3–6, 41–43; PO Sur-Reply 2–6.

We conclude that they do not. In the case of challenged independent claims 1 and 10, the language of the claims expressly define what constitutes an "effective amount." Claim 1 recites:

> A method for treating age related macular degeneration patient in need thereof, comprising intravitreally administering, to said patient, an effective amount of aflibercept *which is* 2 mg approximately every 4 weeks for the first three months, followed by 2 mg approximately once every 8 weeks or once every 2 months.

Ex. 1001, claim 1 (emphasis added). Claim 10 uses virtually identical language. In other words, claims 1 and 10 expressly recite and define an

effective dose as "2 mg approximately every 4 weeks for the first three months, followed by 2 mg approximately once every 8 weeks or once every 2 months." The claims are silent with respect to any additional metric of required efficacy of this effective amount, requiring only the amount delivered at the prescribed intervals.

This is consistent with the disclosures of the '601 Specification. The Specification defines the claim term "therapeutically effective amount" thus:

> As used herein, the phrase "therapeutically effective amount" means a dose of VEGF antagonist that results in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or a dose of VEGF antagonist that inhibits, prevents, lessens, or delays the progression of an angiogenic eye disorder. In the case of an anti-VEGF antibody or a VEGF receptor-based chimeric molecule such as VEGFR1R2-FcΔC1(a) [e.g., aflibercept], a therapeutically effective amount can be from about 0.05 mg to about 5 mg.

Ex. 1001, cols. 6–7, ll. 58–1. The Specification then lists a range of therapeutically effective amounts of VEGF receptor antagonists ranging between 0.5 mg and 5 mg. *Id.* at col. 7, ll. 2–19. In other words, "an effective amount" is defined by the Specification as the *amount* of VEGF receptor antagonist that, when administered in the claimed method, will "result[] in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or … inhibit[], prevent[], lessen[], or delay[] the progression of an angiogenic eye disorder." *Id.* at col. 6, ll. 61–65.

A person of ordinary skill in the art would thus understand that "an effective amount" is defined by the language of the claims as the amount of VEGF receptor antagonist that will cause the disclosed effects. Nothing in the language of the claims, or in the disclosures of the '601 Specification, expressly requires determining a degree of efficacy, rather, the claims are

directed to a prescribed regimen of drug administration. We conclude that a person of ordinary skill, understanding the disclosures of the Specification, would understand that the amounts of VEGF receptor antagonist recited in the claims and disclosed in the Specification constitute a "therapeutically effective amount" without additionally requiring a "high level of efficacy" comparable to that achieved by monthly doses of Lucentis or Avastin.

Furthermore, our -00881 Decision came to a similar conclusion, rejecting 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, second alteration in original). 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).

With respect to challenged independent claim 34, we arrive at a conclusion similar to that concerning claims 1 and 10. Claim 34 does not expressly recite "an effective amount which is…" as do claims 1 and 10, but recites only "an effective sequential dosing regimen." For the same reasons that we have explained above, we construe this to refer to a sequential dosing regimen administered at the intervals recited in the claim, with the dosage amount being within the range (0.5–5.0 mg) disclosed in the '601 Specification that will "result[] in a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or … inhibit[], prevent[], lessen[], or delay[] the progression of an angiogenic eye disorder." *See* Ex. 1001, col. 6, ll. 60–65.

Our reviewing court's decision in *Eli Lilly and Co. v. Teva Pharms. Int'l GmbH*, 8 F.4th 1331 (Fed. Cir. 2021) supports our reasoning that the challenged claims do not require a "high level of efficacy" as Patent Owner argues. In *Eli Lilly*, the court upheld the Board's conclusion that the preamble of the claims at issue reciting "a method for treating headache in an individual" was limiting upon the claims. *Eli Lilly*, 8 F.4th at 1335, 1343.

The *Eli Lilly* claims also recited "administering to the individual an effective amount," similar to the language of the challenged claims of the present *inter partes* review. *Id.* at 1335. The court approvingly noted, in upholding the Board's conclusion, that the Board "found that while the claims encompass a clinical result, they do not *require* such a result." *Id.* at 1343. We also find that the similar language of the preamble to the challenged claims of the '601 patent, and the recitation of an "effective amount" or "an effective sequential dosing regimen," although encompassing clinical efficacy, does not *require* it, let alone a "high degree of efficacy."

Patent Owner argues that, without requiring a degree of efficacy, challenged claim 34 would encompass administering infinitesimal quantities of VEGF antagonist, incapable of achieving any treatment efficacy. *See* PO CC Opp. 2. We disagree. Challenged claims 1 and 10 expressly recite what constitutes an effective dose. With respect to challenged claim 34, as we have explained above, the '601 Specification sets forth a series of exemplary dosage ranges that would constitute a "therapeutically effective amount" generally being encompassed with the range of 0.5–5.0 mg of aflibercept. A person of ordinary skill in the art, reading the claims in light of the Specification would understand that these therapeutically effective amounts are those that would be expected to produce the results described by the Specification, *viz.*, "a detectable improvement in one or more symptoms or indicia of an angiogenic eye disorder, or … inhibit[], prevent[], lessen[], or delay[] the progression of an angiogenic eye disorder." *See* Ex. 1001, col. 6, ll. 60–65.

Finally, Patent Owner argues that if "the Board finds that the challenged claims require some non-zero level of efficacy other than that

advanced by Patent Owner, it will be a new construction, neither advocated nor addressed by either party." PO CC Opp. 5. We do not do so here because we do not require *any* degree of efficacy to be imported into the claims. Rather, we construe the claim terms "effective amount" in challenged claims 1 and 10 to be the amount (2 mg) recited in the claims administered at the recited dosage intervals. We construe the claim term "effective sequential dosing regimen" of claim 34 to mean "administration of a VEGF receptor inhibitor at the recited dosage intervals and in the amount disclosed by the Specification (i.e., 0.5–5.0 mg) as being therapeutically effective."

2. The exclusion criteria

The "exclusion criteria" limitation of challenged claims 9 and 36 recites: "wherein exclusion criteria for the patient include (1) active intraocular inflammation; or (2) active ocular or periocular infection." *See, e.g.*, Ex. 1001, col. 21, ll. 65–67.

a. Petitioner's arguments

Petitioner argues that the "exclusion criteria" are entitled to no patentable weight under the printed matter doctrine. Pet. 23.

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). Pet. 23. 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. 24. 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.* 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. 24–25. 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. 15. According to Patent Owner, the exclusion criteria are not mere "informational content," and a skilled artisan would understand that they are not optional when practicing the claimed methods. *Id.* at 16 (citing Ex. 2056 ¶¶ 95–99). 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 '601 Specification confirms that the exclusion criteria are mandatory. PO Resp. 17. 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 recited exclusion criteria of the claims, and were employed in Example 4. *Id.* (citing Ex. 1001, cols. 10–12, ll. 50–32; Ex. 2056 ¶¶ 91, 96). 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.*

Patent Owner asserts that both parties' experts confirm that a person of ordinary skill in the art would understand that the exclusion criteria are mandatory. PO Resp. 17. 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.* (quoting Ex. 2330 ¶¶ 93, 203, 251; Ex. 2323, 105–109). Patent Owner notes that its expert, Dr. Do, agrees with Dr. Albini's testimony. *Id.* at 18 (citing Ex. 2056 ¶¶ 97, 98). Patent Owner contends that the mandatory character 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 ¶ 99; 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.* (citing Ex. 2062, 3) (alteration in original).

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. 18 (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.* at 19 (citing Ex. 1001, cols. 21, ll. 65–67, col. 24, ll. 22–24; Ex. 2323, 104–105, 123).

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. 19. 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. *Id.* 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 v. Dement*, 254 F.3d 1053, 1058–60 (Fed. Cir. 2001); *Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d 1349, 1356–57 (Fed. Cir. 2014); *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333–34 (Fed. Cir. 2003); *GlaxoSmithKline LLC v. Fibrogen, Inc.*, IPR2016-01318, 2017 WL379248, at *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. PO Resp. 20 (citing Ex. 2056 ¶ 90). As an instance of this, Patent Owner points again to Example 4 of the ’601 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.* (citing Ex. 2056 ¶¶ 91–96, 108; Ex. 1001, col. 12, ll. 56–64, 41–48). Patent Owner argues that such assessments are a routine part of clinical practice as well. *Id.* at 24 (citing Ex. 1002 ¶ 98; Ex. 2323, 122, 72–82, 92, 99–100, 123).

Patent Owner also argues that the doctrine of claim differentiation also supports the conclusion that the exclusion criteria of challenged claims 9 and 36 are limiting. PO Resp. 22. Patent Owner contends that claims of a patent are presumed to have a difference in scope, particularly where the "the absence of such difference in meaning and scope would make a claim superfluous." *Id.* (quoting *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998)).

Specifically, Patent Owner contends that the exclusion criteria are the sole difference between Claims 9 and 36 and the claims from which they depend (Claims 8 and 35, respectively). PO Resp. 22. According to Patent Owner, the doctrine of claim differentiation supports finding that the recited exclusion criteria limitation narrows the scope of challenged claims 9 and 36 compared to claims 8 and 35, from which they depend, by restricting the population of patients who may be treated according to the claimed methods. *Id.* (citing, e.g., *Littlefuse, Inc. v. Mersen USA EP Corp.*, 29 F.4th 1376, 1380 (Fed. Cir. 2022)).

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

Petitioner replies that, in addition to the Board's preliminary finding that the exclusion criteria lack patentable weight, the district court in the parallel *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.) (the "district court proceedings") arrived at the same conclusion in its *Markman* order that the exclusion criteria in the '601 patent's claims 9 and 36 claims lack patentable weight. Pet. Reply 7.

Petitioner also disputes Patent Owner's contention that unlike contraindications printed on a drug label, a skilled artisan would not treat the

exclusion criteria as optional in clinical practice. Pet. Reply 8 (citing PO Resp. 18). Petitioner points out that Patent Owner's expert, Dr. Do, acknowledges that a person of ordinary skill in the art "could, in his or her discretion," elect to perform an injection on a patient who presents with intraocular inflammation." *Id.* (Ex. 2056 ¶ 99; Ex. 1107 ¶ 65).

Petitioner argues that, under *Praxair*, claims 9 and 36 are "informational" because they ask doctors merely to think about the question instead of changing the dosing method. Pet. Reply 8 (citing Ex. 1112, 30–31). Petitioner asserts that the dose, drug, and schedule that the '601 patent recites does not change based on the outcome of reading, knowing, or thinking about any patient inflammation/infection information. *Id.* (citing Ex. 1112, 31). Furthermore, contends Petitioner, the exclusion criteria language does not require the practitioner to take any action at all. Rather, argues Petitioner, if the exclusion criteria are met, the method will not be practiced at all; the claimed steps of dosing 2 mg aflibercept on the regimen schedule recited in challenged independent claims 1 and 34 remains unaltered. *Id.* at 8–9 (citing Ex. 1112, 32, 33).

Consequently, argues Petitioner, the mental step of deciding not to treat a patient is unpatentable because "[o]nce the information is detected, no … treatment is given." Pet. Reply 9 (citing *INO Therapeutics LLC v. Praxair Distrib. Inc.*, 782 F. App'x 1001, 1008 (Fed. Cir. 2019)) (alteration in original). Petitioner points to the district court's *Markman* order, which found 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.* at 9–10 (quoting Ex. 1112,

35). The district court also found that "[t]his distinguishes the claims here from *Praxair* claim 9, where the method was required to start, then it could be modified based on the information." *Id.* at 10 (quoting Ex. 1112, 32). Petitioner also points to our Institution Decision's preliminary conclusion that "there is no direction to the practitioner to perform, or not perform, any specific step based upon the provided criteria." *Id.* (quoting Dec. 15).

Patent Owner responds that although Petitioner cites Dr. Do's testimony on physician discretion in clinical practice, this has no bearing on whether the exclusion criteria are mandatory when practicing the challenged claims. Patent Owner acknowledges that treating physicians can administer aflibercept in any number of ways within their medical judgment, but such administration will only practice claims 9 and 36 if it meets every limitation, including by applying the exclusion criteria. PO Sur-Reply 7 (citing, e.g., Ex. 2056 ¶ 99). Patent Owner points out that both parties' experts agree that applying the exclusion criteria requires the active step of patient assessment to identify a treatment-eligible patient. *Id.* at 7–8 (citing Ex. 2323, 72–79).

Patent Owner also argues that the evidence of record supports its contention that a skilled artisan would understand that the exclusion criteria must be applied, not merely considered. PO Sur-Reply 8. Patent Owner asserts that there is no discretionary or informational component to Claims 9 and 36. *Id.*

Patent Owner contends that the exclusion criteria also define the treatment-eligible patient population, and that if the exclusion criteria were ignored, the method would treat a different (broader) group of patients. PO Sur-Reply 8. Consequently, argues Patent Owner, the exclusion criteria bear a functional relationship to the rest of the claim and should be accorded

patentable weight. *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.* at 9.

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 does not apply only to literal printed matter, but, rather, is applicable when a claim limitation "claims the content of information." *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 *In re 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)) (alteration in original).

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) (holding 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 (1) active intraocular inflammation; or (2) active ocular or periocular infection." This listing of conditions relays direct information to the practitioner of the patent 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 analogous to claim 1 in *Praxair*, in which the practitioner of the claimed "method of providing pharmaceutically acceptable nitric oxide gas" included providing 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.

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. 18. 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 all of the steps of the claimed method.

To be clear, and contrary to Patent Owner's position, we find that 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 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 patent's 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 arguing that, by listing the exclusion criteria, challenged claims 9 and 36 of the '601 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.

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 1329,

1333–34 (alteration in original). 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 '601 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 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 identical exclusion criteria limitations in Patent Owner's '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)) (emphasis omitted, alteration in original).

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:

> 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.

Paper 98 ("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, 33–34 (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 does not result in a manipulative difference in the steps of the claim, and are therefore not functionally related to the claim.

Finally, Patent Owner argues that, under the doctrine of claim differentiation, claims are presumed to have a difference in their scope, and that the exclusion criteria, by excluding certain patients from the method,

further restrict the scope of the claims from which they depend. PO Resp. 22. We find that Patent Owner's argument begs the question by assuming, *a priori*, that the exclusion criteria are entitled to patentable weight because, Patent Owner argues, they restrict the scope of the claims. We disagree with Patent Owner's position because, as we have explained, we find that the limitations do *not* limit the claim, because they require no action (or inaction) on the part of the practitioner of the claimed method, but are informational in nature. Consequently, the exclusion claims of challenged claims 9 and 36 do not alter the scope of the claims from which they depend because they have no patentable weight.

We consequently conclude that the exclusion criteria of the challenged claims are not entitled to patentable weight under the printed matter doctrine.

3. The Best Corrected Visual Acuity limitations

Dependent challenged claims 5 and 6 recite limitations concerning the Best Corrected Visual Acuity requirements (the "BCVA limitation") for the claimed method. Claim 5 is exemplary and recites "wherein the patient gains at least 15 letters of Best Corrected Visual Acuity (BCVA) score." Ex. 1001, col. 21, ll. 55–56.

a. Petitioner's argument

In its Reply Brief, Petitioner argues that the BCVA limitation does not change the manipulative steps of the claims, and should therefore also be construed to have no patentable weight. Pet. Reply 11 (citing Ex. 1112, 38–39).

Petitioner argues that Patent Owner acknowledges that there is no change that doctors can make to the claimed regimen to ensure a particular BCVA score is achieved. Pet. Reply 11 (citing PO Resp. 26). Petitioner analogizes challenged claims 5 and 6 to the claims at issue in *Bristol-Myers*, in which the additional claim elements involved tumor regression and reducing patient toxicity, whereas the dosing schedule remained the same. *Id.* (citing *Bristol-Myers*, 246 F.3d at 1375–76). Petitioner notes that the Federal Circuit explained that the added claim language reflected "only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claim." Therefore, the court concluded, the language was not limiting on the claim. *Id.* (quoting *Bristol-Myers*, 246 F.3d at 1376; also citing *Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018); *King Pharms.*, 616 F.3d at 1277–79 (holding that adding test score outcomes to a method where patient blood AUC and other test measurements did not change the manipulative steps of the claim were non-limiting); also citing Ex. 1112, 37–39).

b. Patent Owner's position

Patent Owner first argues that The Board should disregard Petitioner's argument that the BCVA limitations lack patentable weight, because it exceeds the proper scope of a Reply Brief. PO Sur-Reply 10 (citing USPTO, *Consolidated Trial Practice Guide* at 45 (Nov. 2019)).

Patent Owner also argues that nothing about the BCVA limitations constitutes printed matter or mental steps. PO Sur-Reply 10. Patent Owner notes that, in a related proceeding, *Apotex Inc. v. Regeneron Pharms., Inc.*, IPR2022-01524 (PTAB Mar. 10, 2023), the Board considered and rejected

this argument, finding that such visual acuity gain limitations (or "results limitations") "must be given patentable weight." *Id.* (quoting *Apotex*, IPR2022-01524, Paper 9 at 18).

Specifically, Patent Owner asserts that, in *Apotex*, the Board found that the limitation reciting "wherein the patient achieves a gain in visual acuity within 52 weeks following the initial dose" was limiting upon the challenged claims. PO Sur-Reply 11 (citing *Apotex*, IPR2022-01524, Paper 9 at 18). Patent Owner notes that, in so finding, the Board considered, but did not find persuasive, the same case law Petitioner relies on in its Reply Brief, and found that the BCVA limitations aligned more closely with those held patentable in *Los Angeles Biomedical Research Inst. at Harbor-UCLA Med. Center v. Eli Lilly & Co.*, 849 F.3d 1049 (Fed. Cir. 2017). *Id.* (citing *Apotex*, IPR2022-01524, Paper 9 at 16–18). According to Patent Owner, the Board noted that, similarly to the claims in *LA Biomed*, the challenged claims were "directed to administering a pharmaceutical (aflibercept) to patients in need thereof, at a specified regimen and dosage, where a result of that treatment is expressly recited in the body" of the claims. *Id.* (quoting *Apotex*, IPR2022-01524, Paper 9 at 16).

Patent Owner contends that the BCVA limitations of challenged claims 5 and 6, like those addressed in *Apotex* and *LA Biomed*, are standalone limitations that "demand[] efficacy." PO Sur-Reply 12 (citing *Apotex*, IPR2022-01524, Paper 9 at 17; *LA Biomed*, 849 F.3d at 1061) (alteration in original). Patent Owner asserts that it is undisputed between the parties that the claims' requirement that "the patient gains at least 15 letters of [BCVA]" is not met unless the patient receiving the dosing regimen does, in fact, experience the required visual acuity gain. *Id.* (citing

Ex. 2347, 99–102). It is similarly undisputed, argues Patent Owner, that this gain does not occur in every patient. *Id.* (citing Ex. 2347, 100–101; Ex. 2323, 156). Accordingly, Patent Owner contends, the BCVA limitation gives the challenged claims "meaning and purpose" by adding an additional condition for success. *Id.* (citing *Griffin v. Bertina*, 285 F.3d 1029, 1033 (Fed. Cir. 2002)).

Patent Owner thus distinguishes the BCVA limitations from the unpatentable recitations of efficacy in *Bristol-Myers* and *Copaxone*, which were not standalone limitations, but preambles, and which were duplicative of other claim elements. PO Sur-Reply 12–13 (citing *Bristol-Myers*, 246 F.3d at 1375; *Copaxone*, 906 F.3d at 1022–23).

c. Analysis

As an initial matter, we decline to heed Patent Owner's urging that we disregard Petitioner's arguments as being improperly first raised in the Reply Brief. *See* PO Sur-Reply 10. Whether the BCVA limitations are limiting upon the claims is certainly relevant to our construction of the challenged claims in this *inter partes* review, and as long as Patent Owner has received notice of, and had an opportunity to be heard with respect to, a proposed claim construction (even one raised *sua sponte* by the Board) Patent Owner's procedural rights under the Administrative Procedures Act are not violated. *Qualcomm Inc. v. Intel Corp.*, 6 F.4th 1256, 1265 (Fed. Cir. 2021). In this instance, Patent Owner received notice of Petitioner's proposed construction in its Reply Brief, and had an opportunity to be heard, both in its Sur-Reply Brief and at oral argument. *See, e.g.*, PO Sur-Reply 10–13; Hearing Tr. 66–68. Furthermore, the issue having been raised by

Petitioner's Reply Brief, Patent Owner could also have requested authorization for additional briefing upon the issue, which it did not. Consequently, we look to the merits of the parties' competing claim constructions.

Nevertheless, and as we explain in Section IV.C.4.b, iii below, we need not reach the question of whether the BCVA limitations of claims 5 and 6 are limiting, because we conclude that Dixon inherently discloses the BCVA limitations.

4. "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. 22. 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. 42–52. 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. 22 (citing Ex. 1001, col. 3, ll. 62–67; Ex. 1002 ¶¶ 44–45).

Patent Owner does not dispute Petitioner's construction.

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 "secondary doses" 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. 42–52.

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. 25–26. 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 26 (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 1–9, 34–39, 41–43, 45 by Dixon (Ex. 1006)

Claims 1–9, 34–39, 41–43, and 45 of the '601 patent are challenged by Petitioner as unpatentable under 35 U.S.C. § 102 as being anticipated by Dixon. Pet. 43–50.

1. Overview of Dixon

Dixon was published in October 2009, and is prior art to the '601 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.* at 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.*

Relevantly, 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 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. Petitioner's arguments

a. Challenged claims 1 and 34

Petitioner presents the following tables summarizing its argument that the challenged independent claims are anticipated by Dixon:

For claim 1:

Claim 1	Dixon
A method for treating age related macular degeneration in a patient in need thereof,	"VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and Phase II trial data indicating safety, tolerability and efficacy for the treatment of neovascular AMD." (Ex. 1006, 1573, 1577). Phase 2 patients "treated with 2.0 mg or 0.5 mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p<0.0001$) and 5.4 ($p < 0.085$) ETDRS letters with 29 and 19%

	gaining, respectively, ≥ 15 ETDRS letters at 52 weeks." (*Id.*, 1576). "Two Phase III studies in wet AMD [VIEW1/VIEW2] are currently under way and seek to compare monthly ranibizumab to monthly or bimonthly VEGF Trap-Eye." (*Id.*, 1577–78).
comprising intravitreally administering, to said patient,	"The safety, tolerability and biological activity of intravitreal VEGF Trap-Eye in treatment of neovascular AMD was evaluated in the two-part Clinical Evaluation of Anti-angiogenesis in the Retina-1 (CLEAR-IT-1) study." (*Id.*).
an effective amount of aflibercept which is 2 mg	Patients treated with monthly loading doses of 2.0 mg followed by PRN dosing "achieved mean improvements of 9.0…ETDRS letters with 29%...gaining… ≥ 15 ETDRS letters at 52 weeks." (*Id.*, 1576). Patients in this arm also displayed mean decreases in retinal thickness of 143 μM compared to baseline. (*Id.*) "One promising new [angiogenesis inhibiting] drug is aflibercept (VEGF Trap-Eye), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2." (*Id.*, 1573 (Abstract)). "VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure." (*Id.*, 1575).
approximately every 4 weeks for the first 3 months, followed by 2 mg approximately once every 8 weeks or once every 2 months.	"[Phase 3] will evaluate the safety and efficacy of . . . 2.0 mg at an 8 week dosing interval (following ***three monthly doses***)." (Ex. 1006, 1576 (emphasis added)).

Pet. 43–45. For claim 34:

Claim 34	Dixon
A method for treating an angiogenic eye disorder in a patient in need thereof,	"VEGF Trap-Eye is a novel anti-VEGF therapy, with Phase I and Phase II trial data indicating safety, tolerability and efficacy for the treatment of neovascular AMD." (Ex. 1006, 1573, 1577). Phase 2 patients "treated with 2.0 mg or 0.5 mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p<0.0001$) and 5.4 ($p < 0.085$) ETDRS letters with 29 and 19% gaining, respectively, ≥ 15 ETDRS letters at 52 weeks." (*Id.*, 1576). "Two Phase III studies in wet AMD [VIEW1/VIEW2] are currently under way and seek to compare monthly ranibizumab to monthly or bimonthly VEGF Trap-Eye." (*Id.*, 1577–78).
said method comprising administering to the patient an effective sequential dosing regimen of 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	"[Phase 3] will evaluate the safety and efficacy of . . . 2.0 mg at an 8 week dosing interval (***following three monthly doses***)." (Ex. 1006, 1576 (emphasis added)). In other words, an "initial dose" at day 0, "secondary doses" at weeks 4 and 8; and "tertiary doses" of every 8 weeks beginning at week 16 (i.e., doses at weeks 0, 4, 8, 16, 24, 32, 40, and 48).
wherein each secondary dose is administered 4 weeks after the	(*Id.*). (i.e., the doses at weeks 0, 4, 8).

immediately preceding dose; and	
wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;	(*Id.*). (i.e., the doses at weeks 16, 24, 32, 40, and 48).
wherein the VEGF antagonist is a receptor-based chimeric molecule comprising an immunoglobin-like (Ig) domain 2 of a first VEGF receptor which is VEGFR1 and an Ig domain 3 of a second VEGF receptor which is VEGFR2, and a multimerizing component.	VEGF Trap-Eye is "a fusion protein of binding domains of VEGF receptors-1 and -2 attached to the Fc fragment of human IgG." (Ex. 1006, 1576 (Fig.1)). "VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure." (*Id.*, 1575).

Pet. 45–46.

b. Challenged claims 2, 8, 42, and 43

Petitioner argues that these dependent claims further claim neovascular (wet) AMD or AMD. Pet. 46. Petitioner points to Dixon's disclosure of administering VEGF Trap-Eye to patients with neovascular AMD. *Id.* (citing Ex. 1006, 1573, 1576 ("~1200 patients with neovascular AMD"); Ex. 1002 ¶¶ 158–160, 184–186).

c. Challenged claims 3 and 4

Claims 3 and 4 recite "wherein the patient loses less than 15 letters of Best Corrected Visual Acuity (BCVA) score" and "wherein Best Corrected

Visual Acuity (BCVA) is according to Early Treatment Diabetic Retinopathy Study (ETDRS) letter score." Pet. 47.

Petitioner asserts that Dixon discloses that in phase 2 "[p]atients initially treated with 2.0 … mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p < 0.0001$) … ETDRS [BCVA] letters with 29[%] … gaining … ≥ ~15 ETDRS letters at 52 weeks."[15] Pet. 47 (citing Ex. 1006, 1576) (alterations in original). According to Petitioner, a gain of ≥ ~15 ETDRS BCVA letters necessarily encompasses a loss of less than 15 letters. *Id.* (citing Ex. 1002 ¶ 162). Petitioner also contends that Dixon discloses that for phase 3 (VIEW) "the primary outcome will be the proportion of patients who maintain vision at week 52 (defined as a loss of < 15 ETDRS letters)." *Id.* (citing Ex. 1006, 1576; Ex. 1002 ¶ 162).

Petitioner additionally argues that the claimed visual acuity measures do not distinguish the claimed dosing regimens from prior art disclosing the same regimens. Pet. 47. Claim 1 (from which claims 3 and 4 depend) covers the dosing regimen used in the VIEW trial; the same dosing regimen was disclosed in Dixon. *Id.* (citing Ex. 1002 ¶ 163). Petitioner argues that "because the prior art methods in their 'normal and usual operation … perform the function which [PO] claims in [the '601 patent], then such [patent] will be considered, to have been anticipated by the [prior art].'" *Id.* at 47–48 (quoting *King Pharms.*, 616 F.3d at 1276 (quoting *In re*

[15] We note here that, similar to challenged claims 5 and 6, claims 3 and 4 appear to recite the BCVA limitations that we concluded in Section IV.A.3.c *supra* are not eligible to be accorded patentable weight. However, because Petitioner does not make this argument with respect to claims 3 and 4, we set forth Petitioner's arguments on the merits as presented in its Petition.

Ackenbach, 45 F.2d 437, 439 (C.C.P.A. 1930)) (alteration in original); and citing *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1380 (Fed. Cir. 2005).

d. Challenged claims 5 and 6

Challenged claims 5 and 6 recite "wherein the patient gains at least 15 letters of Best Corrected Visual Acuity (BCVA) score" and "wherein Best Corrected Visual Acuity (BCVA) is according to Early Treatment Diabetic Retinopathy Study (ETDRS) letter score."

Petitioner argues that Dixon discloses that in phase 2 "[p]atients initially treated with 2.0…mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p < 0.0001$)…ETDRS [BCVA] letters with 29[%]…gaining…≥ ~15 ETDRS letters at 52 weeks." N Pet. 48 (citing Ex. 1006, 1576; Ex. 1002 ¶ 167).

Petitioner additionally contends that, as with claims 3 and 4, Dixon discloses that the same VIEW clinical trial regimen with the same drug now claimed in claim 1, from which claims 5 and 6 depend, and thus that Dixon necessarily anticipates these claims. Pet. 48 (citing Ex. 1002 ¶¶ 168–69; *King Pharms.*, 616 F.3d at 1276; *Perricone*, 432 F.3d at 1380.

e. Claim 7

With respect to claim 7, which recites "wherein approximately every 4 weeks comprises approximately every 28 days or approximately monthly," Petitioner argues that Dixon discloses "[Phase 3] will evaluate the safety and efficacy of…2.0 mg at an 8 week dosing interval (following three monthly

doses)." Pet. 48–49 (citing Ex. 1006, 1576; Ex. 1002 ¶¶ 154–157) (alterations in original).

f. Challenged claims 9 and 36

Claims 9 and 36 recite "wherein exclusion criteria for the patient include (1) active intraocular inflammation; or (2) active ocular or periocular infection." Pet. 49. Patent Owner contends that the recited exclusion criteria are entitled no patentable weight, an argument with which we agree, as we explain in Section IV.A.2.d above. *Id.* Consequently, we do not reach Petitioner's additional arguments with respect to these claims.

g. Challenged claim 35

Claim 35 limits the claimed method of claim 34 to "aflibercept." Petitioner argues again that Dixon discloses that "VEGF Trap-Eye and aflibercept (the oncology product) have the same molecular structure," and are therefore the same molecule. Pet. 49 (citing Ex. 1006, 1575). Petitioner also points to Dixon's disclosure that "[o]ne promising new [angiogenesis inhibiting] drug is aflibercept (VEGF Trap-Eye), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2." *Id.* (citing Ex. 1006, 1573 (Abstr.); Ex. 1002 ¶ 172) (emphasis omitted, second alteration in original).

h. Challenged claims 37 and 38

Claims 37 and 38 recite "intraocular administration" and "intravitreal administration." Petitioner contends that intravitreal administration is a subset of intraocular administration and refers to administration directly into

the vitreous chamber of the eye. Pet. 50 (citing Ex. 1002 ¶¶ 69, 179; Ex. 1001, col. 2, ll. 47–50). Petitioner also notes that Dixon discloses that the VIEW studies will evaluate "the safety and efficacy of intravitreal VEGF Trap-Eye." *Id.* (citing Ex. 1006, 1576).

i. Challenged claims 39, 41, and 45

Claims 39, 41, and 45 recite "recite "2 mg" of VEGF antagonist. Petitioner asserts that Dixon discloses the use of 2.0 mg VEGF Trap-Eye doses with the VIEW dosing regimen. Pet. 50 (citing Ex. 1006, 1576 ("2.0 mg at an 8 week dosing interval (following three monthly doses")); Ex. 1002 ¶¶ 181–183). According to Petitioner, Dixon explains that the 2 mg intravitreal dose "allows for extended blocking of VEGF in the eye, but would be predicted to give negligible systemic activity as it will be rapidly bound to VEGF and inactivated." *Id.* (citing Ex. 1006, 1575).

3. Patent Owner's Response

Patent Owner first argues, again, that because Petitioner's references do not disclose any efficacy data for the claimed method for treating, either expressly or inherently, the claims are not anticipated. PO Resp. 23 (citing, e.g., *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1055 (Fed. Cir. 2010); *Novartis Pharms. Corp. v. Accord Healthcare, Inc.*, No. 18-1043-KAJ, slip op. at 37 (D. Del. Aug. 10, 2020)). Patent Owner argues further that, because the recited method for treating is not the necessary result of carrying out the disclosures set forth in Dixon, Petitioner cannot show this limitation is inherently present. *Id.* at 23–24.

Patent Owner also argues that Dixon discloses only prospective studies "designed to evaluate the efficacy and safety of VEGF Trap-Eye" administered according to a specified dosing regimen. PO Resp. 24 (citing Ex. 1013, 1). According to Patent Owner, Dixon does not disclose the high level BCVA gains required by the method of Claims 5 and 6. *Id.* (citing Ex. 1001, col. 21, ll. 55–59; Ex. 2056 ¶¶ 36, 39, 42, 44; Ex. 2323, 197–202, 208). Nor, argues Patent Owner, does Dixon otherwise disclose "any data showing that the claimed Q8 dosing regimen would effectively treat." *Id.* (citing Ex. 2056 ¶¶ 36, 39, 42, 44; Ex. 2323, 197–202).

Patent Owner next argues that the visual acuity gains required by the BCVA limitations of challenged claims 5 and 6 do not necessarily result from the disclosures of the prior art. PO Resp. 25–29.

Patent Owner next contends that, even if a person of ordinary skill in the art knew how to make VEGF Trap-Eye, due to the inherent variability in protein production, such a skilled artisan would not necessarily produce a version of the protein that could treat an angiogenic eye disorder according to the claimed dosing regimen. PO Resp. 29 (citing Ex. 2057 ¶¶ 116–119; Ex. 2096, 90–91). According to Patent Owner, variations in fusion protein production may result in misfolding, aggregation, truncation due to proteolytic cleavage, and/or various changes in covalent post-translational modifications, which can affect the stability and biological activity of recombinant proteins. *Id.* (citing Ex. 2057 ¶¶ 118–119; Ex. 2097, 3–4). Patent Owner argues that for glycoproteins, changes in host cell and culture conditions were known to greatly affect the pattern and extent of post-translational glycosylation of the expressed protein. *Id.* (citing Ex. 2057 ¶ 121). Patent Owner contends that the presence and quantity of sialic acid

residues incorporated post-translationally into a protein were known to affect "absorption, serum half-life, and clearance from the serum, as well as the physical, chemical and immunogenic properties of the respective glycoprotein." *Id.* at 29–30 (citing Ex. 2057 ¶ 122 (quoting Ex. 2099, 1)).

Patent Owner argues that given the variability of manufacturing therapeutic biologics, knowing how to make VEGF Trap-Eye would not necessarily result in a protein that effectively treated an angiogenic eye disorder according to the claimed method. PO Resp. 30 (citing Ex. 2099 ¶ 131; also citing *Rapoport*, 254 F.3d at 1063; *Galderma Labs., L.P. v. Teva Pharms. USA, Inc.*, 799 F. App'x 838, 845–46 (Fed. Cir. 2020)).

Patent Owner argues further that the disclosed dosing regimen will not necessarily result in treating angiogenic eye disorders in some patients. PO Resp. 31. According to Patent Owner, even if VEGF Trap-Eye were made correctly, properly purified, and formulated, administration according to the disclosed regimen will not necessarily result in an effective treatment for all patients with angiogenic eye disorders. *Id.* Petitioner's expert posits that if the claims require efficacy, they require "a loss of 15 or fewer letters on the ETDRS visual acuity chart." *Id.* (citing Ex. 1002 ¶ 52). Patent Owner does not agree that a regimen resulting in vision loss would be considered effective treatment by 2011, nevertheless, it maintains that Petitioner has not shown inherency even under that standard.

Patent Owner argues that, because administration of VEGF Trap-Eye under the claimed dosing regimen will not *necessaril*y result in effectively treating a patient with angiogenic eye disease, Petitioner cannot demonstrate inherency. PO Resp. 31 (citing, e.g., *Galderma*, 799 F. App'x at 846; *Rapoport*, 254 F.3d at 1063).

Finally, Patent Owner argues that, with respect to Petitioner's argument that its references anticipate the challenged claims because "anticipation does not require actual performance" and "proof of efficacy is not required," Supreme Court precedent that experimental uses (like the prospective VIEW trials) do not constitute prior art should apply with equal force to printed publications that disclose such experimental uses. PO Resp. 33 (citing *City of Elizabeth v. Am. Nicholson Pavement Co.*, 97 U.S. 126, 134–35 (1877)). Patent Owner contends that non-secret use of an invention for experimental purpose is not anticipatory if the inventor retains control of the invention. *Id.* (citing *City of Elizabeth*, 97 U.S. at 134–35). Patent Owner notes that this doctrine has been applied to the initiation of clinical trials. *Id.* (citing, e.g., *Eli Lilly & Co. v. Zenith Goldline Pharms.*, 471 F.3d 1369, 1380–81 (Fed. Cir. 2006)).

Patent Owner contends that the disclosure in Dixon of the initiation and design of trials—studies for which Regeneron retained control—does not, therefore, anticipate the challenged claims because the trials were experiments to perfect the invention. PO Resp. 33 (citing *In re Omeprazole Pat. Litig.*, 536 F.3d 1361, 1372–75 (Fed. Cir. 2008)).

4. Analysis

a. Challenged independent claims 1 and 34

We conclude that Petitioner has demonstrated, by a preponderance of the evidence, that the challenged claims of the '601 patent are anticipated by Dixon.

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 claims 1 and 34 of the present challenged claims and claim 1 of the '338 patent in the -00881 Decision. Differences between the challenged claims and claim 1 of the '338 patent are indicated in italics:

IPR2022-01226 US 10,888,601 B2 Claim 1	**IPR2022-01226 US 10,888,601 B2 Claim 34**	**IPR2021-00881 US 9,254,338 B2 Claim 1 (unpatentable)**
1. A method for treating *age related macular degeneration* in a patient *in need thereof*	34. A method for treating an angiogenic eye disorder in a patient *in need thereof*,	1. A method for treating an angiogenic eye disorder in a patient,
Comprising *intravitreally* administering, to *said* patient, *an effective amount of aflibercept*	said method comprising administering to the patient *an effective sequential dosing regimen* of 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;
which is 2 mg approximately every 4 weeks for *the first 3 months*, *followed by 2 mg approximately* once every 8 weeks or once every 2 months	wherein each secondary dose is administered 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 receptor-based chimeric molecule comprising *an immunoglobin-like (Ig) domain 2 of a first VEGF receptor which is VEGFR1 and an Ig domain 3 of a second VEGF receptor which is VEGFR2, and a multimerizing component.*	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.

As should be readily apparent to the reader, challenged claims 1 and 34 of the present Petition and claims 1 of the ’338 patent are substantially the same. The independent claims of the ’601 patent require treating a patient “in need thereof,” whereas the preamble of claim 1 of the ’338 patent merely requires treating a patient. However, the slight difference in this preambular language does not functionally alter the claimed method of treatment in any of the claims.[16]

[16] Claim 1 of the ’601 patent more narrowly describes treating patients with age-related macular degeneration rather than an “angiogenic eye disorder.” However, it was well-known in the art that age-related macular degeneration is a species of angiogenic eye disorder, and Dixon expressly discloses the use of aflibercept in the treatment if age-related macular degeneration. *See* Ex. 1001, col. 1, ll. 31–60; Ex. 1006, generally.

Similarly, the challenged independent claims of the ’601 patent require “an effective amount” or “an effective sequential dosing regimen.” We have explained, in Section IV.A.3.f above, that we construe the terms “an effective amount” and “an effective sequential dosing regimen” to mean, respectively, “the amount (2 mg) recited in claim 1 administered at the recited dosage intervals” and “administration of a VEGF receptor inhibitor at the recited dosage intervals and in the amount disclosed by the Specification (i.e., 0.5–5.0 mg) as being therapeutically effective” and not as requiring a “high degree of efficacy,” as argued by Patent Owner. Claim 1 of the ’601 patent additionally recites a 2 mg dose of aflibercept administered at the intervals common to all of the claims. Dixon expressly teaches administration of 2 mg of aflibercept at these intervals. *See* Ex. 1006, 1576 (e.g., “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)).

Finally, claim 34 of the ’601 patent recites a genus of VEGF antagonist which includes the species of VEGF antagonist recited in claim 1 of the ’388 patent and disclosed by Dixon. *See* Ex. 1006, 1575, 1576 (Fig. 1).

Because we concluded, in the -00881 Decision, 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 independent challenged claims 1 and 14 of the ’601 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.

With respect to Patent Owner's arguments in the present *inter partes* review, as an initial matter, we have explained, in Sections IV.A.2–3 above, why we conclude that the exclusion criteria and the BCVA limitations are not limiting upon the claims and are entitled to no patentable weight. Consequently, we do not reach Patent Owner's arguments with respect to the exclusion criteria of claims 9 and 36 or the BCVA limitations of challenged claims 5 and 6.

Similarly, we have explained why we reject Patent Owner's arguments that the language of the claims requires a "high degree of efficacy" that is noninferior to the "standard of care," which was Lucentis or off-label Avastin, and we consequently are not persuaded by Patent Owner's arguments attempting to import any such requirement into the challenged claims. *See supra* Section IV.A.1.f.

We fail to see the relevance of Patent Owner's arguments that knowing how to make VEGF Trap-Eye would not necessarily result in treatment or that even if VEGF Trap-Eye were successfully synthesized, the

disclosed dosing regimen will not necessarily result in treating angiogenic eye disorders in some patients. *See* PO Resp. 29–32. The challenged claims of the '601 patent are not directed to a method of synthesizing VEGF Trap-Eye, or claim the compound itself. Rather, the challenged claims recite of administering the compound to a patient. As such, the method is directed to the dosage regimen. Dixon expressly discloses the claimed method of administration of VEGF Trap-Eye to a patient. Furthermore, and as we explain in Section IV.A.1.f above, we reject Patent Owner's contention that the claims require a high degree of efficacy in *any* patient. Rather the claims are directed to the method of administration of the drug.

Finally, with respect to Patent Owner's arguments that Dixon does not anticipate the challenged claims because it describes an experimental use, we considered this argument in the -0881 Decision and rejected it. *See* Ex. 3001, 44–45. Briefly, in considering this question, the Board emphasized that Dixon is a printed publication that discloses each element of the claimed invention. *Id.* at 44. In particular, the reference discloses treating an angiogenic eye disorder by administering VEGF-Trap Eye according to the dosing regimen recited by the challenged claims to the patient, concluding that "[a]nti-VEGF therapy has vastly improved the treatment of neovascular AMD in terms of both safety and efficacy." *Id.* at 44–45 (citing Ex. 1006, 1576) (alteration in original). Based on those disclosures, the Board found that the intended purpose of the claimed methods is to treat an angiogenic eye disorder and that such treatment only requires administering the recited dosing regimen to a patient for that purpose, without any requirement that such treatment achieves any particular level of efficacy. *Id.* at 45.

We adopt the same reasoning here, and conclude that Patent Owner has not established that Dixon is unavailable as anticipatory prior art because Dixon did not disclose an unclaimed feature for the method of treating, i.e., a particular level of effectiveness. Patent Owner's argument is, consequently, not persuasive.

b. Challenged dependent claims 2–9, 35–39, 41–43, and 45

As an initial matter, and for the reasons we have explained in Sections IV.A.2.f respectively, challenged dependent claims 9 and 36 recite the exclusion criteria as their sole limitation. Because we conclude that this limitation cannot be accorded patentable weight, these claims share the fate of dependent claims 8 and 35, from which they depend and which we address below.

i. Challenged claims 2, 8, 42, and 43

These claims all require that the angiogenic eye disorder to be treated is age-related macular degeneration. Claims 2 and 8 further require that the age-related macular degeneration be neovascular (wet), and claim 43 lists age-related macular degeneration as one of a number of angiogenic eye disorders. *See* Ex. 1001, claims 2, 8, 42, 43.

Dixon expressly discloses treating patients with neovascular (i.e., "wet") age-related macular degeneration. Ex. 1006, 1573, 1576 ("The first part, VIEW 1 (VEGF Trap: Investigation of Efficacy and safety in wet age-related macular degeneration) will enroll ~1200 patients with neovascular AMD"). Patent Owner does not dispute this disclosure of Dixon, and we

conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claims 2, 8, 42, and 43.

ii. Challenged claims 3 and 4

Challenged claims 3 and 4 recite, respectively, "wherein the patient loses less than 15 letters of Best Corrected Visual Acuity (BCVA) score" and "wherein Best Corrected Visual Acuity (BCVA) is according to Early Treatment Diabetic Retinopathy Study (ETDRS) letter score." Ex. 1001, claims 3, 4.

Dixon discloses that in phase 2, "[p]atients initially treated with 2.0 . . . mg of VEGF Trap-Eye monthly achieved mean improvements of 9.0 ($p < 0.0001$) … ETDRS [BCVA] letters with 29[%] … gaining … ≥ ~15 ETDRS letters at 52 weeks." (Ex. 1006, 1576). Petitioner contends, and Patent Owner does credibly not dispute, that a gain of ≥ ~15 ETDRS BCVA letters necessarily encompasses a loss of less than 15 letters. Pet. 47 (citing Ex. 1002 ¶ 162). Dixon also discloses that for phase 3 (VIEW) "the primary outcome will be the proportion of patients who maintain vision at week 52 (defined as a loss of < 15 ETDRS letters)." *Id.* (citing Ex. 1006, 1576; Ex. 1002 ¶ 162).

We therefore conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claims 3 and 4.

iii. Challenged claims 5 and 6

Dixon also inherently discloses the BCVA limitations. A reference may anticipate inherently if a claim limitation that is not expressly disclosed "is necessarily present, or inherent, in the single anticipating reference."

Verizon Servs. Corp. v. Cox Fibernet Va., Inc., 602 F.3d 1325, 1337 (Fed. Cir. 2010). As we have explained Dixon discloses the claimed 2Q8 dosing regimen. Example 6 of the '601 Specification discloses that "at Week 52, 55.3% of VEGFT-treated patients gained ≥15 letters vs 30.1 % of sham-treated patients (P <0.01). At Week 52, VEGFT-treated patients gained a mean of 16.2 letters vs 3.8 letters for sham-treated patients (P <0.001)." Ex. 1001, col. 15, ll. 14–18; *see Arbutus Biopharma Corp. v. ModernaTX, Inc.*, 65 F.4th 656, 664 (Fed. Cir. 2023) ("To anticipate, the prior art need only meet the inherently disclosed limitation to the same extent as the patented invention"); *see also King Pharms.*, 616 F.3d at 1275. Consequently, a person of ordinary skill in the art, following the method disclosed by Dixon, would have necessarily achieved the results recited in claims 5 and 6, and challenged claims 5 and 6 are thus inherently disclosed by Dixon.

iv. Challenged claim 7

Challenged claim 7 recites "wherein approximately every 4 weeks comprises approximately every 28 days or approximately monthly." Ex. 1001, claim 7.

Dixon discloses "[Phase 3] will evaluate the safety and efficacy of…2.0 mg at an 8 week dosing interval (following three monthly doses)." Ex. 1006, 1576. Patent Owner does not dispute this disclosure of Dixon, and we conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claim 7.

v. Challenged claim 35

Challenged claim 35 recites "the VEGF antagonist is aflibercept." Ex. 1001, claim 7.

Dixon discloses that "[o]ne promising new drug is aflibercept (VEGF Trap-Eye), a fusion protein that blocks all isoforms of VEGF-A and placental growth factors-1 and -2." Ex. 1006. Abstr. Dixon further discloses that VEGF Trap-Eye, the active agent in its disclosed AMD studies, and aflibercept, "have the same molecular structure," although there are variations in the formulation (i.e., further purification and differences in buffers) of VEGF Trap-Eye employed in the vision studies, to make it compatible with intravitreal injection. *Id.* at 1575.

We conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claim 35.

vi. Challenged claims 37 and 38

Challenged claims 37 and 38 recite "wherein all doses of the VEGF antagonist are administered to the patient by intraocular administration" (claim 37) or by "intravitreal administration," (claim 38) which is a type of intraocular administration. Ex. 1001, claims 37 and 38; *see also* Ex. 1002 ¶¶ 69, 179; Ex. 1001, col. 2, ll. 47–50 (describing intravitreal administration as a species of intraocular administration).

Dixon discloses that that "all anti-VEGF agents for neovascular AMD are administered only by intravitreal injection." Ex. 1006, 1574. Dixon also discloses that "the low intravitreal dose of 2 mg allows for extended blocking of VEGF in the eye, but would be predicted to give negligible systemic activity." *Id.* at 1575. Dixon further discloses that the VIEW

study, which embodies the claimed method of the '601 patent, will evaluate "the safety and efficacy of intravitreal VEGF Trap-Eye." *Id.* at 1576. Patent Owner does not dispute these disclosures of Dixon.

We therefore conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claims 37 and 38.

vii. Challenged claims 39, 41, and 45

Challenged claims 39, 41, and 45 all recite administered doses of "about 2 mg" (claim 39) or "2 mg" (claims 41, 45) VEGF antagonist. Ex. 1001, claims 39, 41, 45.

Dixon discloses that a 2 mg intravitreal dose "allows for extended blocking of VEGF in the eye, but would be predicted to give negligible systemic activity as it will be rapidly bound to VEGF and inactivated." Ex. 1006, 1575. Dixon further discloses that, in the VIEW study, "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)" are administered. *Id.* at 1576. Patent Owner does not dispute these disclosures.

We consequently conclude that Petitioner has demonstrated, by a preponderance of the evidence, that Dixon anticipates claims 39, 41, and 45.

V. CONCLUSION

For the reasons we have explained, we conclude that Petitioner has demonstrated, by a preponderance of the evidence, that challenged claims 1–9, 34–39, 41–43, and 45 of the '601 patent are unpatentable as being anticipated by Dixon (Ground 1). Because we conclude that all of the

challenged claims are thus anticipated, we do not reach the additional Grounds 2–7 proposed in the Petition. 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 1–9, 34–39, 41–43, and 45 of the '601 patent are unpatentable;

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

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

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.

Ground	Claims	35 U.S.C. §	Reference(s)/ Basis	Claims Shown Unpatentable [17]	Claims Not shown Unpatentable
1	1–9, 34–39, 41–43, 45	102	Dixon	1–9, 34–39, 41–43, 45	
2	1–9, 34–39, 41–43, 45	102	Adis		
3	1–9, 34–39, 41–43, 45	102	Regeneron 2008		
4	1–9, 34–39, 41–43, 45	102	NCT-795		
5	1–9, 34–39, 41–43, 45	103	Dixon, Papadopoulos ,Wiegand		
6	1–9, 34–39, 41–43, 45	103	Dixon, Rosenfeld-2006, Papadopoulos , Wiegand		
7	1–9, 34–39, 41–43, 45	103	Dixon, Heimann-2007 Papadopoulos , Wiegand		
	Overall Outcome			1–9, 34–39, 41–43, 45	

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

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