Trials@uspto.gov
571-272-7822

Paper 21
Date: January 11, 2023

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,

Patent Owner.

IPR2022-01225
Patent 10,130,681 B2

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

NEW, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner Mylan Pharmaceuticals Inc. ("Petitioner") has filed a Petition (Paper 2, "Pet.") seeking *inter partes* review of claims 1, 3–11, 13, 14, 16–24, and 26 of US Patent 10,130,681 B2 (Ex. 1001, the "'681 patent"). Patent Owner Regeneron Pharmaceuticals, Inc. ("Patent Owner") timely filed a Preliminary Response. Paper 14 ("Prelim. Resp."). With our authorization (*see* Paper 16 at 1), Petitioner filed a Reply to the Preliminary Response (Paper 16 ("Reply")), and Patent Owner filed a Sur-Reply. Paper 18 ("Sur-Reply").

Under 35 U.S.C. § 314, the Board "may not authorize an *inter partes* review to be instituted unless … the information presented in the petition … and any response … shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." Upon consideration of the Petition, Preliminary Response, Reply, Sur-Reply, and the evidence of record, we determine that the evidence presented demonstrates a reasonable likelihood that Petitioner would prevail in establishing the unpatentability of at least one challenged claim of the '681 patent.

II. BACKGROUND

A. Real Parties-in-Interest

Petitioner identifies Viatris Inc., Mylan Inc., Mylan Pharmaceuticals Inc., Momenta Pharmaceuticals, Inc., Janssen Research & Development LLC, and Johnson & Johnson as the real parties-in-interest. Paper 8 at 1. Patent Owner identifies Regeneron Pharmaceuticals, Inc. as the real party-in-interest. Paper 5 at 1.

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B. Related Matters

Petitioner and Patent Owner identify *Mylan Pharms. Inc. v. Regeneron Pharms., Inc.*, IPR2021-00880, IPR2021-00881, IPR2022-01226 (PTAB), and *Regeneron Pharms., Inc. v. Mylan Pharms. Inc.*, 1:22-cv-00061-TSK (N.D.W. Va.). as related matters. Paper 5 at 1; Paper 6 at 1. Patent Owner also identifies *Chengdu Kanghong Biotechnology Co. v. Regeneron Pharms., Inc.*, PGR2021-00035 (PTAB) (proceeding terminated). Paper 5 at 2–3. Petitioner further identifies the following as judicial or administrative matters that would affect, or be affected by, a decision in this proceeding: *Apotex Inc. v. Regeneron Pharmaceuticals, Inc.*, No. IPR2022-01524 (PTAB), *United States v. Regeneron Pharms., Inc.*, No. 1:20-cv-11217-FDS (D. Mass.), and *Horizon Healthcare Servs., Inc. v. Regeneron Pharms., Inc.*, No. 1:22-cv-10493-FDS (D. Mass.). Paper 6 at 1–2.

Petitioner also identifies additional patents and patent applications that claim priority to the ’681 patent, namely: US 9,254,338 B2; US 9,669,069 B2; US 10,857,205 B2; US 10,828,345 B2; US 10,888,601 B2; 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 at 2.

Of particular relevance to our decision in this proceeding is the Final Written Decision entered in IPR2021-00881 on November 9, 2022. *See* IPR 2021-00881, Paper 94 (the “-00881 Decision” Ex. 3001). Both the ’681 patent and US 9,254,338 B2 (the “’338 patent”) in IPR2021-00881 share a common Specification. *See generally*, Ex. 1001, IPR2021-00881, Ex. 1001. In the -00881 Decision, the panel found that the challenged claims were

unpatentable on at least one of the same grounds asserted against the challenged claims in the present Petition. *See generally* Ex. 3001.

C. The Asserted Grounds of Unpatentability

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

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1	1, 3–11, 13, 14, 16–24, 26	102[1]	Dixon[2]
1	1, 3–11, 13, 14, 16–24, 26	102	Adis[3]
3	1, 3–11, 13, 14, 16–24, 26	102	Regeneron 2008[4]

[1] 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.

[2] 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.

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

[4] 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.

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Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
4	1, 3–11, 13, 14, 16–24, 26	103	Dixon alone or in view of Papadopoulos[5] and/or Wiegand[6]
5	1, 3–11, 13, 14, 16–24, 26	103	Dixon in combination with Rosenfeld-2006[7], and if necessary, Papadopoulos patent and/or Wiegand
6	1, 3–11, 13, 14, 16–24, 26	103	Dixon in combination with Heimann-2007, and if necessary, Papadopoulos and/or Wiegand

Petitioner also relies upon the Declarations of Dr. Thomas A. Albini (the "Albini Declaration," Ex. 1002) and Dr. Mary Gerritsen (the "Gerritsen Declaration," Ex. 1003). Patent Owner relies upon the Declaration of Dr. Diana V. Do (the "Do Declaration," Ex. 2001).

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

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

[7] 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.

D. The '681 Patent

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

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

E. Representative Claim

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

> 1. A method for treating an angiogenic eye disorder in a patient, said method comprising sequentially administering to the patient a single initial dose of a VEGF antagonist, followed by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;
>
> wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and
>
> wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
>
> wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a

> VEGFR2 component comprising amino acids 130-231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232-457 of SEQ ID NO:2;
>
> wherein exclusion criteria for the patient include all of:
>
> (1) active intraocular inflammation;
>
> (2) active ocular or periocular infection;
>
> (3) any ocular or periocular infection within the last 2 weeks.

Ex. 1001, col. 21, ll. 40–63.

F. Priority History of the '681 Patent

The '681 patent issued from U.S. Application Ser. No. 15/471,506 (the "'506 application") filed on March 28, 2017, and claims the priority benefit of, *inter alia*, US Provisional Application Ser. No. 61/432,245, which was filed on Jan. 13, 2011. Ex. 1001, code (60).

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

III. 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

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meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317 (quoting *C.R. Bard, Inc. v. U.S. Surgical Corp.*, 388 F.3d 858, 862 (Fed. Cir. 2004)).

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

Patent Owner disagrees, arguing that not only is the preamble limiting and requires "treating," but that the recited "method for treating" requires "a high level of efficacy." Prelim. Resp. 21–30. Patent Owner further contends that the recited "initial," "secondary," and "tertiary dose" limitations similarly require achieving and maintaining a high level of efficacy. *Id.* at 30–37. Finally, Patent Owner argues that the printed matter doctrine is inapplicable to the "exclusion criteria" limitation and that this

limitation is limiting upon the claims. *Id.* at 38–44. We address each of these arguments in turn.

1. Preamble

Petitioner argues the preamble is not limiting upon the claims. Pet. 17–18. Petitioner argues that: (1) the preamble is merely a statement of intended purpose and, therefore, not a limitation; and (2) the preamble provides no antecedent basis for any other claim element, and that any argument that "the patient" and "angiogenic eye disorder" claim terms find their respective meaning in the preamble is meritless. *Id.* at 20. Alternatively, argues Petitioner, if the preamble is limiting, it should be given its plain and ordinary meaning, which does not require any specific efficacy requirement. *Id.* at 20–23.

Patent Owner responds that: (1) the preamble is limiting and requires "treating"; (2) the recited "method for treating" requires a high level of efficacy; and (3) the intrinsic record supports a high level of efficacy. Prelim Resp. 21–30.

These same arguments were argued and addressed in the prior -00881 Decision. *See* Ex. 3001, 12–23. In the -00881 Decision, challenged claim 1 of US 9,254,338 B2 (the "'338 patent") recited preamble language identical to that recited in claim 1 of the '681 patent, *viz.*, "a method for treating an angiogenic eye disorder in a patient." *See* Ex. 1001 col. 21, ll. 40–41; Ex. 3001, 7. The Board found that this preamble was limiting upon the remainder of the claim. Ex. 3001, 18. Specifically, the Board found that:

> Here, the claims are directed to methods of administering, i.e., using, a VEGF antagonist for an intended purpose of "treating an

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

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

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

> [W]hen the Specification explains that "[t]he amount of VEGF antagonist administered to the patient in each dose is, in most cases, a therapeutically effective amount," and discloses that "a therapeutically effective amount can be from about 0.05 mg to about 5 mg," we find that a POSA would have understood that any dosage amount within that range administered according to

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> the invention may, in some cases, result in a detectable improvement in "one or more symptoms or indicia of an angiogenic eye disorder," or be one that "inhibits, prevents, lessens or delays the progression of an angiogenic eye disorder," or it may not. In either event, the VEGF antagonist would have been administered for the purpose of treating the eye disorder. In other words, the method of treating the patient with the eye disorder is performed upon administration of the VEGF antagonist to the patient for the purpose of achieving an improvement or beneficial effect in the eye disorder, regardless whether the dosage amount administered actually achieves that intended result.

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

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

Id. at 22 (citations omitted).

We adopt the same reasoning here, and find that, for the purposes of this Decision, the evidence of record and the Specification support construing the preamble's recitation of a "method for treating a patient with an angiogenic eye disorder" as meaning administering a compound, i.e., the recited VEGF antagonist, to such patient for the purpose of improving or providing a beneficial effect in their angiogenic eye disorder, but does not

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require a "high level of efficacy," as proposed by Patent Owner. *See* Ex. 3001, 22.

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

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

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

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

Patent Owner responds that the claim terms "initial," "secondary," and "tertiary dose" again require achieving and maintaining a high level of efficacy. Prelim. Resp. 30. According to Patent Owner, if these claim terms implied only a temporal sequence, the challenged claims would encompass

administering ineffective doses of VEGF antagonist—e.g., infinitesimal quantities that are incapable of achieving any efficacy. This would be an incongruous interpretation of claims directed to a "method for treating" angiogenic eye disorders. *Id.*

Furthermore, argues Patent Owner, when the claims are considered as a whole, it is evident that the dosing regimen recited in the claims—i.e., less frequent "tertiary dose(s)" following more frequent "initial" and "secondary" doses—must actually "treat[]" the angiogenic eye disorder for which the VEGF antagonist is being administered, and such treatment must be comparable in efficacy to standard-of-care Lucentis and off-label Avastin. Prelim. Resp. 32.

We are persuaded that Petitioner proposes the more correct 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. 36–44.

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

> Based on those express definitions in the Specification, we do not find cause to construe the terms differently. In particular, we do not find that the Specification requires the "tertiary doses" to maintain any efficacy gain achieved after the initial and

> secondary doses, or that the term suggests any specific level of efficacy. *The Specification unequivocally states that "[t]he terms 'initial dose,' 'secondary doses,' and 'tertiary doses,' refer to the temporal sequence of administration of the VEGF antagonist*."

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

3. The exclusion criteria

The exclusion criteria limitation of challenged claim 1 recites:

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

(1) active intraocular inflammation;
(2) active ocular or periocular infection;
(3) any ocular or periocular infection within the last 2 weeks.

Ex. 1001 col. 21, ll. 58–62. Petitioner argues that the "exclusion criteria" are entitled to no patentable weight under the printed matter doctrine. Pet. 25.

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

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whether the printed material is "interrelated with the rest of the claim." *Id.* Printed matter that is functionally related to its substrate is given patentable weight. *Id.* (citing *DiStefano*, 808 F.3d at 850).

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

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

Patent Owner responds that, in the -00881 Decision, the Board determined that the substantially identical preamble is a positive limitation

because it defines (in part) who is treated (a patient with an angiogenic eye disorder). Prelim. Resp. 39 (citing Ex. 3001, 16–19 (finding that the preamble "method of treating an angiogenic eye disorder" is limiting)). Patent Owner argues that the "wherein" clause of the exclusion criteria limitation further limits who may be treated with the claimed method—not only must the patient suffer from an angiogenic eye disorder, but also must not meet any of the recited exclusion criteria. *Id.* Therefore, contends Patent Owner, the exclusion criteria serve to limit the population of patients on whom the claimed method may be performed. *Id.* at 39–40.

Patent Owner asserts that it is well-established that claim terms defining the population of patients to be treated with a claimed method are limiting. Prelim. Resp. 40 (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 WL 379248, *3 (PTAB Jan. 11, 2017); also citing *Praxair*, 890 F.3d at 1035). According to Patent Owner, claim limitations that define the treated patient population also define how (i.e., upon whom) the treatment steps are performed, and that if one were to ignore the exclusion criteria when practicing the claimed method steps, a different (broader) group of patients would be treated. *Id.* Consequently, argues Patent Owner, the exclusion clause of the challenged claims modify and further specify the "patient" of the preamble. *Id.* at 41.

Turning to the two-part analysis of *Praxair*, Patent Owner argues that the exclusion criteria are not directed to any communication of information (printed or otherwise) so as to "claim[] the content of information," and

therefore do not meet the first step one of the printed matter inquiry. Prelim Resp. 41 (quoting *Praxair*, 890 F.3d at 1031–32). Patent Owner notes that, in *Praxair*, the claims at issue held to contain printed matter were expressly directed to "providing information" or a "recommendation" to the medical provider, which the medical provider was free to ignore. Prelim. Resp. 42 (citing *Praxair*, 890 F.3d at 1028–30). To the contrary, Patent Owner argues, in the present proceeding, nothing in the challenged claims is directed to the mere provision of information, and there is consequently no "ineligible information" in the claims to begin with. *Id.* (citing *Praxair*, 890 F.3d at 1033).

Turning to the second step of the *Praxair* test, Patent Owner contends that the exclusion criteria define the patient population to be treated, and so are a limitation with patentable weight. Prelim. Resp. 42. Patent Owner analogizes the challenged claims to claim 9 in *Praxair*, which the court found did not comprise unpatentable printed matter, because it further required the medical provider to take a specific action—discontinuing treatment—as a result of the recommendation limitation. *Id.* (citing *Praxair*, 890 F.3d at 1035). Consequently, Patent Owner points out, the printed matter of claim 9 was functionally related to body of the claim and had patentable weight. *Id.* Similarly, argues Patent Owner, the present challenged claims require the recited administering steps to be performed only on patients who do not meet the exclusion criteria, creating a functional relationship with the rest of the claim. *Id.* at 43.

We are persuaded that, for the purpose of this Decision, Petitioner has the better position. In *Praxair*, our reviewing court has 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 *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)).

In the case presently before us, there is little question that the exclusion criteria are directed to informational content. Specifically, the limitation in question expressly states that the "exclusion criteria for the patient include all of: (1) active intraocular inflammation; (2) active ocular or periocular infection; (3) any ocular or periocular infection within the last 2 weeks." This list of conditions relays direct information to the practitioner of the 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 certainly analogous to the 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* Prelim. Resp. 42. However, an individual practicing the method of the challenged claims would be similarly free to ignore the conditions of the exclusionary criteria and still be practicing the claimed method. Granted, the outcome for the patient in either case might well be unfortunate, but there are no positive or negative

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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.

We consequently find, for the purpose of this Decision, that the exclusion criteria are not limiting upon the challenged claims under the printed matter doctrine. The parties may wish to further develop their respective arguments upon this issue at trial.

B. A Person of Ordinary Skill in the Art

Petitioner contends that a person of ordinary skill in the art would have: (1) knowledge regarding the diagnosis and treatment of angiogenic eye disorders, including the administration of therapies to treat said disorders; and (2) the ability to understand results and findings presented or published by others in the field. Pet. 28. Petitioner asserts that such a person would typically have an advanced degree, such as an M.D. or Ph.D. (or equivalent, or less education but considerable professional experience in the medical, biotechnological, or pharmaceutical field), with practical academic or medical experience in (i) developing treatments for angiogenic eye disorders, including through the use of VEGF antagonists, or (ii) treating of same, including through the use of VEGF antagonists. *Id.* at 28–29 (citing Ex. 1002 ¶¶ 27–29; Ex. 1003 ¶¶ 21–25).

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Patent Owner does not expressly contest this definition of a person of ordinary skill in the art in its Preliminary Response. For the purposes of this decision, because we find Petitioner's definition to be consistent with the level of skill in the art (*see, e.g.*, Exs. 1006, 1020), and in the absence of a different proposed definition of the level of skill in the art by Patent Owner, we consequently adopt Petitioner's definition.

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

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

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

IPR2022-01225 US 10,130,681 B2 Claim 1	**IPR2021-00881 US 9,254,338 B2 Claim 1 (unpatentable)**
1. A method for treating an angiogenic eye disorder in a patient,	1. A method for treating an angiogenic eye disorder in a patient,
said method comprising sequentially administering to the patient a single initial dose of a VEGF antagonist,	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;	followed by one or more secondary doses of the VEGF antagonist, followed by one or more tertiary doses of the VEGF antagonist;
wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;	wherein each secondary dose is administered 2 to 4 weeks after the immediately preceding dose; and wherein each tertiary dose is administered at least 8 weeks after the immediately preceding dose;
wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2.	wherein the VEGF antagonist is a VEGF receptor-based chimeric molecule comprising (1) a VEGFR1 component comprising amino acids 27 to 129 of SEQ ID NO:2; (2) a VEGFR2 component comprising amino acids 130–231 of SEQ ID NO:2; and (3) a multimerization component comprising amino acids 232–457 of SEQ ID NO:2.
wherein exclusion criteria for the patient include all of: (1) active intraocular inflammation; (2) active ocular or periocular infection; (3) any ocular or periocular infection within the last 2 weeks.	

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As should be readily apparent to the reader, challenged claim 1 of the present Petition and claim 1 of the ’338 patent are identical, with the sole exception in the ’681 patent of the additional limitation reciting the exclusion criteria. Because, in the -00881 Decision, we concluded that claim 1 of the ’338 patent is anticipated by Dixon, we incorporate here by reference our reasoning in the -00881 Decision with respect to the corresponding limitations of claim 1 of the ’681 patent. *See* -00881 Decision, 26–46. We therefore conclude that Petitioner has demonstrated a reasonable likelihood of prevailing at trial in demonstrating that those limitations of claim 1 of the ’681 are unpatentable as being anticipated by Dixon.

Furthermore, we have explained, in Section III.A.3 above, our reasoning as to why we conclude, for the purpose of this Decision, that Petitioner has demonstrated a reasonable likelihood of establishing that the remaining exclusion criteria limitation is not limiting upon the claims under the printed matter doctrine and, consequently, likely has no patentable weight. We consequently conclude that Petitioner has demonstrated a reasonable likelihood that challenged claim 1 of the ’681 patent is anticipated by Dixon.

Moreover, because we have determined that Petitioner has shown a reasonable likelihood of prevailing at trial in demonstrating that at least one claim is unpatentable on at least one of the stated Grounds, we institute an *inter partes* review of all challenged claims of the ’681 patent, based on all of the grounds identified in the Petition. *See SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018); *PGS Geophysical AS v. Iancu*, 891 F.3d 1354,

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1360 (Fed. Cir. 2018) (interpreting the statute to require "a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition").

D. Discretionary Denial of Institution under 35 U.S.C. § 314(a)

Finally, Patent Owner urges us to exercise our discretion to deny institution of trial under 35 U.S.C. §314(a) under the analysis set forth in *General Plastic Indus. Co. v. Canon Kabushiki Kasha*, IPR2016-01357, 2017 WL 3917706 (PTAB Sept. 6, 2017) (precedential). Prelim. Resp. 4.[8] Under *General Plastic*, when exercising our discretion to deny institution, we may consider a number of factors:

1. whether the same petitioner previously filed a petition directed to the same claims of the same patent;
2. whether at the time of filing of the first petition the petitioner knew of the prior art asserted in the second petition or should have known of it;
3. whether at the time of filing of the second petition the petitioner already received the patent owner's preliminary response to the first petition or received the Board's decision on whether to institute review in the first petition;
4. the length of time that elapsed between the time the petitioner learned of the prior art asserted in the second petition and the filing of the second petition;

[8] In its Preliminary Response, Patent Owner also urged us to exercise our discretion to deny institution under *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, 2020 WL 2126495, *2–3 (PTAB Mar. 20, 2020) (precedential). Prelim. Resp. 12–17. Patent Owner withdrew this argument in its Sur-Reply, and we therefore do not consider it. *See* Sur-Reply 6.

5. whether the petitioner provides adequate explanation for the time elapsed between the filings of multiple petitions directed to the same claims of the same patent;
6. the finite resources of the Board; and
7. the requirement under 35 U.S.C. § 316(a)(11) to issue a final determination not later than 1 year after the date on which the Director notices institution of review.

General Plastic, Paper 19 at 9–10. The purpose of the analysis thus established in *General Plastic* is to deny a Petitioner successive attacks on the claims of a single patent, and profiting from those prior attempts by altering a petition's strategy in response to Patent Owner's and the Board's responses.

Patent Owner argues that Petitioner's alleged delay in filing the present Petition is an attempt to leverage information acquired during the course of IPR2021-00881 to bolster arguments made in the present Petition. Prelim. Resp. 4. According to Patent Owner, Petitioner argues that the exclusion criteria, the only limitation that differentiates the challenged claims from those previously-challenged in IPR2021-00881, should be ignored, rendering the '681 Patent identical to the previously-challenged '338 Patent. *Id.* Patent Owner also argues that, although *General Plastic* addresses circumstances where a petitioner serially challenges the same patent, the Board has signaled a willingness to consider a *General Plastic* argument when, e.g., a second petition challenges a related patent with a common specification to the first challenged patent. *Id.* at 4–5 (citing *Microsoft Corp. v. Uniloc 2017 LLC*, IPR2019-01251, 2019 WL 7000081,

*3 (PTAB Dec. 20, 2019); *Abiomed, Inc. v. Maquet Cardiovascular, LLC*, IPR2017-02134, 2018 WL 1840065, *2–6 (PTAB Apr. 16, 2018)).

Patent Owner voices an urgent concern that institution imposes a tremendous burden on the Board and Patent Owner, and notes that "[t]here may be other reasons besides the 'follow-on' petition context," as is the case here, because "the 'effect … on the … integrity of the patent system'… favors denying a petition even though some claims meet the threshold standards for institution under 35 U.S.C. §§ 314(a) and 324(a)." Prelim. Resp. 6 (quoting PTAB, *Consolidated Trial Practice Guide* at 58 (Nov. 2019), *available at*: https://www.uspto.gov/about-us/news-updates/consolidated-trial-practice-guide-november-2019 (last visited December 20, 2022) ("CTPG").

We decline to exercise our discretion to deny institution under 35 U.S.C. § 314(a). Indeed, we conclude that we need not even approach the multifactor *General Plastic* analysis outlined above. Patent Owner is quite correct that *General Plastic* is directed to instances where a petitioner serially challenges the same patent. *See General Plastic*, Paper 19 at 8. And we also agree with Patent Owner that the '681 patent shares a common Specification with the '338 patent and that the claims of the two patents are very similar. *See* Prelim. Resp. 4. Nevertheless, the very reason that Patent Owner advances for denying institution of *inter partes* review of the challenged claims of the '681 patent, i.e., the "effect … on the … integrity of the patent system," in fact argues forcefully *for* institution in the present case. In the -00881 Decision, we determined that the claims of the '338 patent were unpatentable. The only difference between claim 1 of the '338 patent and challenged claim 1 of the '681 patent is the inclusion in the latter

of the limitation reciting the exclusion criteria. We have explained, in Section III.A.3 above, why we conclude that Petitioner has shown a reasonable likelihood of prevailing at trial in showing that the exclusion criteria are non-limiting upon the ’681 patent and, consequently, lack patentable weight.

In short, we concluded, in the -00881 Decision, that all of the limitations of a claim that is substantially similar to the present challenged claim 1 are unpatentable, with the exception of the exclusion criteria limitation, which Petitioner has credibly demonstrated is likely to be non-limiting upon the claims under the printed matter doctrine. In effect, Patent Owner is asking us to exercise our discretion to deny institution of *inter partes* review of at least one challenged claim that has been previously determined to be unpatentable with the exception of a single limitation, of which Petitioner has demonstrated a reasonable likelihood of lacking patentable weight. We find that the “effect … on the … integrity of the patent system,” of exercising our discretion to deny institution of *inter partes* review of the challenged claims would be, in fact, directly injurious to that integrity because it would deny *inter partes* review of challenged claims that are highly similar to those found unpatentable in a prior proceeding of the Board. Patent Owner will have the opportunity to litigate at trial whether the exclusion criteria limitation is limiting, and also whether that limitation is anticipated by, or obvious over, the prior art cited by Petitioner in Grounds

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1–6. We consequently deny Patent Owner's request to exercise our discretion under § 314(a) to deny institution of *inter partes* review.

IV. CONCLUSION

For the reasons we have explained, we conclude that Petitioner has demonstrated a reasonable likelihood of prevailing in demonstrating that at least challenged claim 1 of the '681 patent is unpatentable as being anticipated by Dixon. Furthermore, because we determine that Petitioner has shown a reasonable likelihood of prevailing at trial in demonstrating that at least one claim is unpatentable on at least one of the stated Grounds, we institute *inter partes* review of all challenged claims of the '681 patent, based on all of the grounds identified in the Petition. *See SAS*, 138 S. Ct. at 1359–60; *PGS*, 891 F.3d at 1360. We additionally deny Patent Owner's request that we exercise our discretion to deny institution under 35 U.S.C. § 314(a).

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED, pursuant to 35 U.S.C. § 314(a), that the Petition for *inter partes* review of the challenged claims of US Patent 10,130,681 B2 is GRANTED with respect to all grounds in the Petition; and

FURTHER ORDERED that *inter partes* review is instituted.

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For PETITIONER:

Paul J. Molino
Deanne M. Mazzochi
Jeff A. Marx
Neil B. McLaughlin
L. Scott Beall
Thomas H. Ehrich
Steven J. Birkos
RAKOCZY MOLINO MAZZOCHI SIWIK LLP
MYL_REG_IPR@rmmslegal.com

For PATENT OWNER:

Deborah E. Fishman
David A. Caine
Alice S. Ho
ARNOLD & PORTER KAYE SCHOLER LLP
RegeneronEyleaIPRs@arnoldporter.com