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Paper No. 16
Date: February 2, 2023

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANDOZ INC.,
Petitioner,

v.

BIOGEN MA INC.,
Patent Owner.

PGR2022-00054
Patent 11,292,845 B2

Before SHERIDAN K. SNEDDEN, CYNTHIA M. HARDMAN, and JAMIE T. WISZ, *Administrative Patent Judges.*

HARDMAN, *Administrative Patent Judge*

DECISION
Denying Institution of Post-Grant Review
35 U.S.C. § 324

I. INTRODUCTION

Petitioner Sandoz Inc. requests post-grant review of claims 1–16 of U.S. Patent No. 11,292,845 B2 ("the '845 patent," Ex. 1001). Paper 1 ("Pet."). Patent Owner Biogen MA Inc. filed a Preliminary Response. Paper 6 ("Prelim. Resp."). The parties also filed authorized additional briefing. *See* Paper 14 ("Pet. Reply"); Paper 15 ("PO Sur-reply").

Considering the arguments and evidence of record, we determine that the Petition does not demonstrate that the '845 patent is eligible for post-grant review, and thus does not demonstrate "that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable." 35 U.S.C. § 324(a). Accordingly, we deny institution of a post-grant review.

A. Real Parties in Interest

Petitioner identifies itself as the real party in interest and Polpharma SA as a privy. Pet. 80.

Patent Owner identifies itself as the real party in interest. Paper 5 (Patent Owner Mandatory Notices), 2.[1]

B. Related Matters

Patent Owner identifies the following U.S. Patent Applications: 60/776,931, 11/711,628, 12/757,305, 15/285,381, 15/596,468, and 17/709,204. Paper 5, 2–3. The parties do not identify any other related matters. *See id.*; Pet. 80.

[1] Paper 5 is not paginated. We treat the cover page of the exhibit as page 1, and assign each page a consecutive number.

C. The '845 Patent (Ex. 1001)

The '845 patent, titled "Methods of Treating Inflammatory and Autoimmune Diseases with Natalizumab," relates to methods of monitoring patients to improve the safety of natalizumab therapy. Ex. 1001, codes (54), (57). Natalizumab is a recombinant antibody used to treat inflammatory and autoimmune diseases such as multiple sclerosis ("MS"), Crohn's Disease ("CD"), and rheumatoid arthritis ("RA"). *Id.* at 1:14–15, 9:26–28, 3:26–29. "There are three known cases of PML [Progressive Multifocal Leukoencephalopathy] occurring during or after administration of natalizumab." *Id.* at 3:29–31. PML "is a severe, rapidly progressive disease that destroys the myelin coating which protects nerve cells" and "occurs almost exclusively in severely immunosuppressed patients." *Id.* at 3:16–19.

PML is caused by a John Cunningham Virus ("JCV") infection of oligodendrocytes. *Id.* at 20:59–60. "JCV is a human polyoma virus that is believed to infect the majority of healthy individuals at an early age," and PML "may result from a primary infection or follow reactivation of latent virus." *Id.* at 20:60–62, 3:23–25.

The specification identifies "a need in the art for determining the relationship between natalizumab treatment and the occurrence of PML and for safer methods of treating patients with natalizumab that take into account the possibility of contracting PML." *Id.* at 3:34–38. Thus,

> the invention provides a method of using natalizumab to treat a patient with an inflammatory or autoimmune disease by administering a pharmaceutically effective amount of natalizumab; monitoring the patient for indicators of progressive, multifocal leukoencephalopathy; and discontinuing the administration of natalizumab in the presence of indicators

> of progressive multifocal leukoencephalopathy; wherein the monitoring improves the safety of the treatment.

Id. at 3:45–53. "In embodiments the monitoring detects seroconversion and/or an increasing titer of JCV in the patient's urine and/or blood." *Id.* at 4:2–4.

D. Illustrative Claim

Petitioner challenges all claims (1–16) of the '845 patent. Claim 1, the only independent claim 1, reads:

> 1. A method of using natalizumab to treat a patient with an inflammatory or autoimmune disease comprising:
>
> (a) administering a pharmaceutically effective amount of natalizumab to the patient;
>
> (b) monitoring the patient for indicators of progressive multifocal leukoencephalopathy (PML), wherein the monitoring comprises detecting seroconversion and/or an increasing titer of JC virus (JCV) antibodies in the patient's blood; and
>
> (c) discontinuing the administration of natalizumab in the presence of seroconversion and/or an increasing titer of JCV antibodies;
>
> wherein the monitoring improves the safety of the treatment.

Ex. 1001, 31:50–32:7.

Claims 2–6 further define the inflammatory or autoimmune disease. *Id.* at 32:8–20. Claims 7–10 and 14 recite additional types of monitoring the patient for PML. *Id.* at 32:21–32, 32:41–43. Claims 11–13 recite dosages and intervals for natalizumab administration. *Id.* at 32:33–40. Claim 15 further defines the step of detecting seroconversion and/or an increasing titer of JCV antibodies, and claim 16 recites further treatment steps where seroconversion and/or an increasing titer of JCV antibodies is detected. *Id.* at 32:44–54.

E. Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–16 are unpatentable on the following three grounds:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1–16	§ 112(a)	Written Description
1–16	§ 101	Patent Eligible Subject Matter
1–16	§ 103	Alroughani,[2] Tysabri[3]

Pet. 6. Petitioner supports its arguments with a declaration from Samuel J. Pleasure, M.D., Ph.D., among other evidence. Ex. 1002.

II. ANALYSIS

A. Claim Construction

We interpret a claim "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b)." 37 C.F.R. § 42.100(b). Under this standard, we construe the claim "in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *Id.*

Petitioner raises two terms for construction: "JC virus (JCV) antibodies" and "seroconversion . . . of JCV antibodies." Pet. 30–33. For purposes of this Decision we need not expressly address the term "JC virus (JCV) antibodies." *See Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1375

[2] Alroughani et al., *Natalizumab treatment for multiple sclerosis: Middle East and North Africa regional recommendations for patient selection and monitoring*, BMC Neurology, 14:27, 2014 ("Alroughani") (Ex. 1006).

[3] TYSABRI (natalizumab) injection, product label, 2013, Biogen Idec Inc. ("Tysabri") (Ex. 1007).

(Fed. Cir. 2019) ("The Board is required to construe 'only those terms . . . that are in controversy, and only to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

Petitioner asserts that the term "seroconversion . . . of JCV antibodies," which appears in claim 1, "should be construed to require obtaining a reliable 'positive' result from a serologic test that excludes false positives." Pet. 32 (citing Ex. 1001, 25:58–64; Ex. 1002 ¶ 93). Patent Owner counters that "[t]he '845 Patent specification expressly defines 'seroconversion,'" and "[t]his definition controls." Prelim. Resp. 12.

We agree with Patent Owner. The '845 patent specification defines "seroconversion" as "the change of a serologic test from negative to positive, indicating the development of antibodies." Ex. 1001, 9:3–5. Petitioner acknowledges this definition, but asserts that "in 2006, at the time the earliest patent application in the priority chain was filed," "there were no established thresholds for JCV positivity . . . and without such thresholds, [serological tests to detect JCV] could produce false positives (e.g., by cross-reacting with BK virus) and false negatives." Pet. 32–33 (citing Ex. 1002 ¶¶ 29, 99–100). Thus, Petitioner asserts, a person of ordinary skill in the art would understand that "'seroconversion . . . of JCV antibodies' requires a test 'indicating the development of antibodies' that is sufficiently accurate to exclude most false positives and false negatives." *Id.* at 33.

We are not persuaded by Petitioner's arguments. First, as Patent Owner points out, the claims themselves "*do not* require any specific serological test or degree of sensitivity or specificity," and "are agnostic as to which of the various available methods known in the art and described in

the specification for measuring JCV antibodies may be used." Prelim. Resp. 12–13. Second, we agree with Patent Owner that Petitioner's construction "impermissibly imports into the claims subjective requirements such as sensitivity, specificity, reliability, accuracy, or some particular rate of false positives or negatives," none of which are "grounded in the intrinsic record." *Id.* at 14, 15.

For purposes of this Decision, we adopt the '845 patent specification's express definition of "seroconversion," i.e., "the change of a serologic test from negative to positive, indicating the development of antibodies." Ex. 1001, 9:3–5.

B. Level of Ordinary Skill in the Art

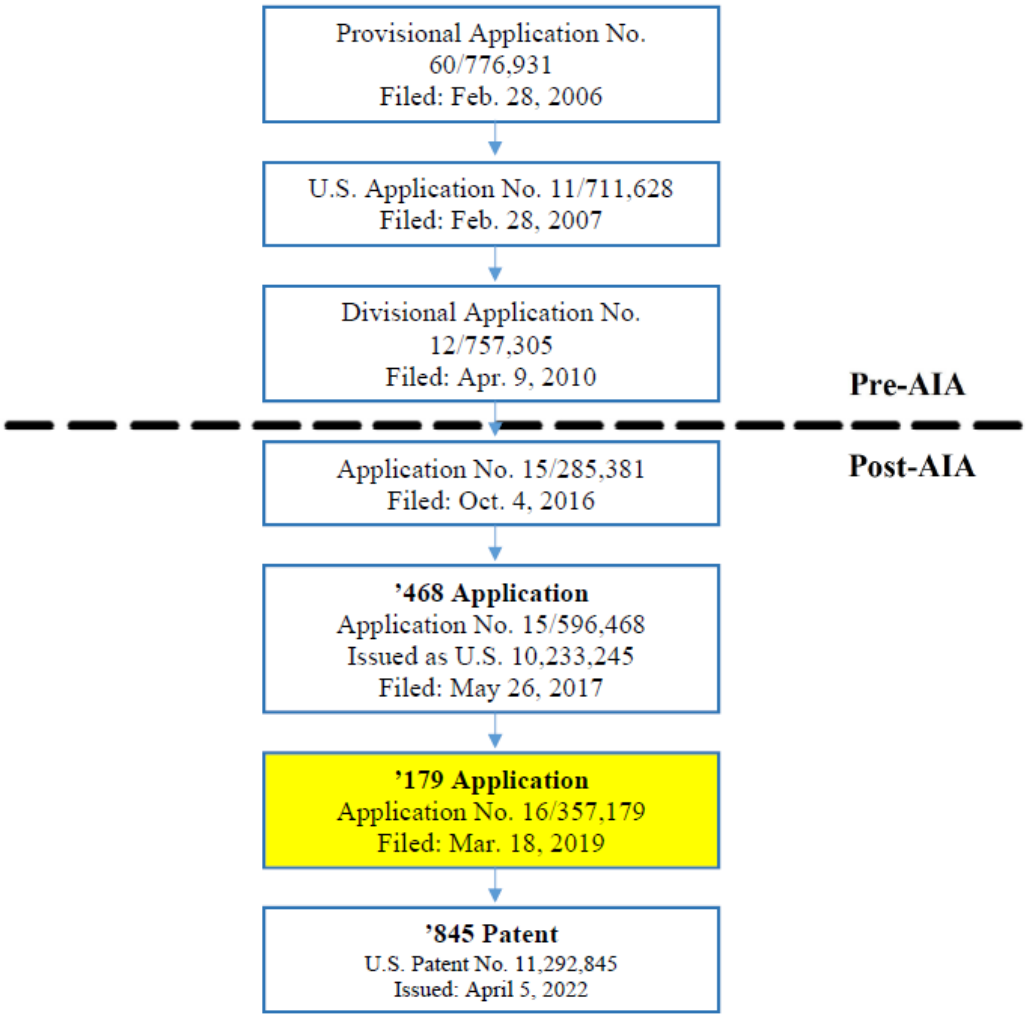
On this record the parties agree that a person of ordinary skill in the art "would have had (1) a Ph.D., M.D., or equivalent degree and (2) at least two years of experience with the use of natalizumab to treat patients with inflammatory or autoimmune diseases, including MS, RA, and/or CD." Pet. 33; Prelim. Resp. 3, n.2. For purposes of this Decision we adopt this undisputed proposal.

C. Post-Grant Review Eligibility

As a threshold matter, we must determine whether Petitioner has shown that the '845 patent is eligible for post-grant review. *See US Endodontics, LLC v. Gold Standard Instruments, LLC*, PGR2015-00019, Paper 17 at 11–12 (PTAB Jan. 29, 2016) (explaining that Petitioner bears the burden of demonstrating that the challenged patent is eligible for post-grant review).

The post-grant review provisions apply to patents that contain or contained at any time a claim with an effective filing date on or after

March 16, 2013. *See* Pub. L. No. 112-29, 125 Stat. 284 (2011), §§ 3(n)(1), 6(f)(2)(A). The '845 patent issued from an application filed on March 18, 2019, and claims priority to a series of applications, the earliest of which was filed in 2006. Ex. 1001, codes (22), (60). To provide context, we reproduce below Petitioner's graphic showing the asserted priority chain of the '845 patent:



Pet. 34. This graphic shows the chain of applications that led to the '845 patent, with a dividing line showing which applications are "pre-AIA," i.e., filed prior to March 16, 2013, and which are "post-AIA," i.e., filed on or

after March 16, 2013. The chain contains three pre-AIA applications, i.e., a provisional application filed in 2006, and two non-provisional applications, namely U.S. Application No. 11/711,628 ("the '628 application"), filed on February 28, 2007, and an application filed in 2010. The chain also contains three post-AIA applications, including an application filed on March 18, 2019, which led directly to the '845 patent.

Petitioner argues that the '845 patent is eligible for post-grant review because the priority applications lack written description support for the '845 patent's claims, thus making the patent's effective filing date March 18, 2019, i.e., the filing date of the application that led directly to the '845 patent.[4] *See* Pet. 35 (citing *PowerOasis, Inc. v. T–Mobile USA, Inc.*, 522 F.3d 1299, 1306 (Fed. Cir. 2008)), 36–55 (detailing asserted deficiencies in written description for the '845 patent's claims). Patent Owner disputes that the '845 patent is eligible for post-grant review, arguing that the pre-AIA priority applications adequately support the claimed methods. *See generally* Prelim. Resp. 22–57.

To determine whether the '845 patent is eligible for post-grant review, we must evaluate whether the required written description support is disclosed in a pre-AIA application and was carried through the subsequent

[4] Entitlement to the benefit of an earlier effective filing date is premised on disclosure of the invention "in the manner provided by [§] 112(a) (other than the requirement to disclose the best mode)" in the earlier application. *See* 35 U.S.C. §§ 119(e), 120. Petitioner's arguments regarding whether the '845 patent is eligible for post-grant review are based solely on an alleged lack of written description support. *See generally* Pet. 33–55. Petitioner does not raise any enablement challenges in the Petition. *See generally id.*; *see also* Pet. Reply 1.

priority chain to the application that led directly to the '845 patent. *See Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1571 (Fed. Cir. 1997) ("In order to gain the benefit of the filing date of an earlier application . . . each application in the chain leading back to the earlier application must comply with the written description requirement."). The parties agree that the specification in the entire non-provisional priority chain is unchanged. *See, e.g.*, Pet. 34–35 ("The pre-AIA, non-provisional patent applications . . . share substantially the same specification as the '845 Patent . . . as the entire non-provisional priority chain consists of continuation applications to which no new matter was added."), 37 n.5 ("The '845 Patent and the '628 Application share the same specification."); Prelim. Resp. 34 n.17. For ease of reference, we cite disclosures in the '628 application and the corresponding disclosures in the '845 patent specification, with the understanding that these disclosures were carried through the intervening applications in the priority chain.[5]

[5] We limit our analysis to the '628 application, which is the first pre-AIA utility application in the priority chain. We do not address the provisional application, because neither party makes substantive arguments regarding the disclosure of that application. For consistency with the parties, our citations to the '628 application are to Exhibit 1025, which is the publication of the '628 application. We note, however, that a written description analysis occurs "as of the filing date sought." *Vas–Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563–64 (Fed. Cir. 1991). Exhibit 1025 published in September 2007, several months after the February 28, 2007 filing date of the '628 application. *See* Ex. 1025, codes (43), (22). Nevertheless, the specification (including the claims) in Exhibit 1025 appears to be unchanged from the specification in the '628 application as filed, which appears in the record as Exhibit 2005. Accordingly, for consistency with the parties, we cite the publication of the '628 application (Exhibit 1025) instead of the '628 application as filed (Exhibit 2005), with the understanding that the

On this record, Petitioner does not persuade us that the '845 patent is eligible for post-grant review.

1. Legal Standard – Written Description

35 U.S.C. § 112(a) requires that a patent's specification "contain a written description of the invention . . . in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010). This provision ensures that as of the filing date "the inventor actually invented the invention claimed." *Id.* at 1350–51. The test "requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.* at 1351.

Adequate description of a genus requires "disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Id.* at 1350. "[F]unctional claim language can meet the written description requirement when the art has established a correlation between structure and function." *Id.*

2. Analysis

Petitioner argues that the '845 patent is PGR-eligible because the challenged claims lack written description support for four independent reasons: (1) claim 1 lacks *ipsis verbis* support in the specification (Pet. 35–36); (2) the priority applications do not support that "monitoring for the

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substantive content of the two specifications is the same. For similar reasons, we cite the '845 patent as issued, rather than the specification of the application filed on March 18, 2019, which led directly to the '845 patent.

presence of JCV serum antibodies would improve the safety of natalizumab treatment" (*id.* at 37); (3) the priority applications do not support that "monitoring *increasing titer* of JCV antibodies in the serum can improve the safety of natalizumab treatment" (*id.* at 47); and (4) the claims "cover the broad, unsupported genus of all classes of JCV antibodies" (*id.* at 49). We address each of Petitioner's arguments, together with Patent Owner's responses, in turn.

a) Alleged Lack of Ipsis Verbis Support

Petitioner asserts that there is no *ipsis verbis* support in the specification for claim 1, particularly for limitation (c), which recites: "discontinuing the administration of natalizumab in the presence of seroconversion and/or an increasing titer of JCV antibodies." *See* Pet. 35–36. Petitioner contends that "the specification's disclosure differs from the language of claim 1, in that [in claim 1,] discontinuation of natalizumab administration is based on the presence of 'seroconversion and/or an increasing titer of JCV antibodies,'" whereas in the specification, it is based on "the more general 'indicators of progressive multifocal leukoencephalopathy,'" such as a PML diagnosis based on detecting JCV DNA in the cerebral spinal fluid. *Id.* at 36.

Petitioner's arguments are not persuasive. In relevant part, claim 1 recites a method of using natalizumab comprising:

> . . . (b) monitoring the patient for indicators of progressive multifocal leukoencephalopathy (PML),
>
> wherein the monitoring comprises detecting seroconversion and/or an increasing titer of JC virus (JCV) antibodies in the patient's blood; and
>
> (c) discontinuing the administration of natalizumab in the presence of seroconversion and/or an increasing titer of JCV antibodies . . . .

Ex. 1001, 31:54–32:6 (spacing added). In other words, step (b) of claim 1 recites monitoring the patient for indicators of PML, and defines those indicators as seroconversion and/or an increasing titer of JCV antibodies. Step (c) of claim 1 recites discontinuing natalizumab if these indicators are present. *See also* Prelim. Resp. 33 (characterizing claimed method); Ex. 1002 ¶ 118 ("Claim 1 of the '845 Patent requires that, after administering natalizumab to the patient, the patient should be monitored 'for indicators of [PML]' by 'detecting seroconversion and/or an increasing titer of JC virus (JCV) antibodies in the patient's blood,' and should 'discontinu[e] the administration of natalizumab in the presence of seroconversion and/or an increasing titer of JCV antibodies.'").

As Patent Owner points out, the method recited in challenged claim 1 is very similar to the method recited in certain original claims in the '628 application. Prelim. Resp. 35–36. In the '628 application as filed, claim 1 recites a step (b) of monitoring the patient for indicators of PML and a step (c) of discontinuing the administration of natalizumab in the presence of indicators of PML, while dependent claim 9 recites that the monitoring "detects seroconversion and/or an increasing titer of JCV in the patient's urine and/or blood." Ex. 1025, claims 1, 7, and 9; *see also Crown Packaging Tech., Inc. v. Ball Metal Bev. Container Corp.*, 635 F.3d 1373,

1380 (Fed. Cir. 2011) ("Original claims are part of the specification and in many cases will satisfy the written description requirement."). This same subject matter is also disclosed in the specification of the '628 application, and was carried through to the '845 patent specification:

> [T]he invention provides a method of using natalizumab to treat a patient with an inflammatory or autoimmune disease by administering a pharmaceutically effective amount of natalizumab; **monitoring the patient for indicators of progressive, multifocal leukoencephalopathy**; and **discontinuing the administration of natalizumab in the presence of indicators of progressive multifocal leukoencephalopathy**; wherein the monitoring improves the safety of the treatment.
>
> . . . In embodiments **the monitoring detects seroconversion and/or an increasing titer of JCV in the patient's urine and/or blood**, and further includes removing a sample of the patient's cerebrospinal fluid when the comparison of the serial urine and/or blood samples detect seroconversion and/or an increasing titer of JCV; and testing the cerebrospinal fluid for the presence of JCV.

Ex. 1025 ¶¶ 15–16 (emphasis added); Ex. 1001, 3:45–4:8. Petitioner does not adequately address these disclosures and their alignment with the language of claim 1.

Petitioner does acknowledge that "the specification discloses detecting seroconversion and/or an increasing titer of 'JCV,'" but argues that this reference to an "increasing titer of JCV" is different than claim 1's recitation of an "increasing titer of JCV *antibodies*." Pet. 36. Petitioner, however, does not persuade us that a person of ordinary skill in the art would have discounted this disclosure in the specification based on an alleged distinction between the phrases "increasing titer of JCV" and "increasing titer of JCV antibodies." Rather, as Patent Owner points out, the '845 patent

specification expressly defines "titer" as "the concentration of an *antibody* in solution." Prelim. Resp. 39 (quoting Ex. 1001, 9:6; emphasis Patent Owner's); *see also* Ex. 1025 ¶ 37 (providing same definition for "titer"). Petitioner fails to account for this express definition in the specification, and also fails to account for surrounding context, such as the two preceding sentences in the specification, which discuss measuring JCV antibodies. Ex. 1001, 3:60–4:2. Accordingly, we agree with Patent Owner that a person of ordinary skill in the art would have understood the specification's reference to an "increasing titer of JCV" as referring to an increasing concentration of JCV antibodies, such that the language of claim 1 aligns with the language of the specification. Prelim. Resp. 39. Notably, the passages of Dr. Pleasure's declaration that Petitioner cites in support of this argument do not address an alleged distinction between the phrases "increasing titer of JCV" and "increasing titer of JCV antibodies." *See* Pet. 36 (citing Ex. 1002 ¶¶ 28–31).

For these reasons, Petitioner has not persuaded us that claim 1 lacks *ipsis verbis* support in the specification.

b) Alleged Lack of Support to Show that Monitoring for the Presence of JCV Serum Antibodies Would Improve the Safety of Natalizumab Treatment

Petitioner asserts that "the specification fails to disclose sufficient written description to show that monitoring for the presence of JCV serum antibodies would improve the safety of natalizumab treatment." Pet. 37; *see also id.* at 44 (arguing that the '845 patent specification "does not provide any support that monitoring JCV serum antibodies would provide the claimed effect of improved safety"). We are not persuaded by Petitioner's argument.

As Patent Owner notes, the priority applications "disclose that monitoring for seroconversion or increasing titer of anti-JCV antibodies, and discontinuing treatment with natalizumab when it is detected, improves the safety of the treatment." Prelim. Resp. 35; *see also* Ex. 1025 ¶¶ 15–16; Ex. 1001, 3:45–4:8. The specification further discloses "monitor[ing] patients receiving natalizumab treatment by routinely assessing them for PML," e.g., once a month. Ex. 1025 ¶ 130; Ex. 1001, 28:12–27. The specification explains that through the monitoring, "[p]atients with possible PML are . . . rapidly identified, so that natalizumab can be immediately discontinued and the proper assessments completed," and that the "monitoring program provides timely information regarding safety issues related to natalizumab." Ex. 1025 ¶ 130; Ex. 1001, 28:17–27. In view of at least these disclosures, Petitioner has not persuaded us that the priority applications lack adequate description to show that the claimed monitoring improves the safety of natalizumab treatment.

We also agree with Patent Owner that many of Petitioner's arguments are not tethered to methods actually claimed by the '845 patent. *See, e.g.*, Prelim. Resp. 44–50. For example, Petitioner argues that there is insufficient written description to show that "monitoring for the *presence* of JCV serum antibodies would improve the safety of natalizumab treatment." Pet. 37 (emphasis added). But challenged claim 1 does not recite monitoring for the mere presence of JCV serum antibodies. Indeed, the specification acknowledges that JCV antibodies are found in the majority of adults, and thus teaches that "monitoring for *changes* in the level of anti-JCV antibodies in a patient taking natalizumab," e.g. by monitoring for "seroconversion and/or an increasing titer" of JCV antibodies, can indicate the risk of PML

and improve the safety of natalizumab treatment. Prelim. Resp. 8–9 (citing, e.g., Ex. 1001, 20:60–62, 25:9–11, 3:62–65, 4:2–4).

As another example, Petitioner's discussion of various statements in the '845 patent specification relating to detecting JCV DNA or determining JCV viral load is divorced from the claimed method. *See* Pet. 39–41 (citing, e.g., Ex. 1001, 13:29–40, 13:55–14:23, 14:52–15:17, 15:30–32, 15:44–46, 21:30–22:6, 23:61–62; Ex. 1002 ¶¶ 41, 45, 96–98). Challenged claim 1 is directed to monitoring for seroconversion and/or an increasing titer of JCV antibodies; it is not directed to monitoring JCV DNA or JCV viral load.

Petitioner argues that the specification (including the two working examples) fails to disclose any actual measurement of JCV antibodies. Pet. 38 (citing, e.g., Ex. 1002 ¶¶ 50, 96–98). This argument is unavailing because "the written description requirement does not demand either examples or an actual reduction to practice." *Ariad*, 598 F.3d at 1352; Prelim. Resp. 43.

Petitioner also asserts that in a prior litigation, Patent Owner admitted that "it had not established that the presence of JCV antibodies would predict the risk of developing PML as of 2007, let alone determined what level of JCV antibodies would serve as a relevant threshold for PML risk." Pet. 38–39 (citing Pet. § IV.E); *id.* at 21–25 (citing Ex. 1005 (Biogen motion for summary judgment); Ex. 1019 (district court order)). This argument is unavailing. First, Petitioner omits relevant context to the litigation. The litigation appears to have concerned allegations that Biogen "acted negligently in not updating the Tysabri label" with "warnings about increased risk of developing . . . [PML]" in patients with JCV antibodies,

and whether the FDA would have "approved a change to the Tysabri label before 2012 to include a warning regarding JCV antibodies." Ex. 1019, 3, 47; Prelim. Resp. 40. The question of whether the FDA would have approved the label change appears to have depended on the availability of "statistically significant" and "clinically validated" data regarding the utility of JCV antibodies. *See* Ex. 1019, 22, 26–27, 47; Prelim. Resp. 40–41; Pet. 3 n.1, 45. Because none of "statistical significance," "clinically validated" data, or FDA approval is required by the challenged claims, these litigation statements, which were made in a very different context, are of questionable relevance.

Second, Petitioner cross-references a section of the Petition that provides a bullet-point list of statements from the prior litigation. *See* Pet. 38–39 (cross-referencing Pet. § IV.E). Petitioner, however, fails to specifically explain how the vast majority of these statements supports its written description and PGR-eligibility arguments. *See id.* Petitioner calls out only two particular statements Patent Owner made in the prior litigation, namely (i) that "[f]rom 2005 through 2009 there was no published literature correlating the risk of PML with the *presence or absence of JCV antibodies* circulating in the bloodstream," and (ii) in 2006 Patent Owner had "no statistically significant data from which to determine whether the *presence* of an antibody would assist in assessing whether someone is at a higher or lower risk of getting PML." *Id.* at 45 (quoting Ex. 1005,[6] 30; Ex. 1019, 22,

[6] For Exhibit 1005, Petitioner appears to be citing the document's native pagination, rather than the pagination Petitioner added to the document for purposes of this proceeding. For consistency, we likewise refer to the native pagination for Exhibit 1005.

25) (emphasis added). Petitioner has not adequately explained how these statements bear on whether the specification adequately supports the claimed method. On their faces, the statements relate to correlating PML risk with the *presence* (or absence) of JCV antibodies, whereas the claims concern detection of *changes* in the antibody levels (seroconversion and/or an increasing titer). Additionally, the first statement relates to the existence of "published literature," not to content within the four corners of the specification, and the second statement relates to "statistically significant data," which is not required by the claimed method. Prelim. Resp. 40–41.

Petitioner's suggestion that this case is similar to four prior Board cases is unavailing. Pet. 42–44, 48–49. The claims in each of those cases concern compounds or compositions having a particular claimed function. *See Syngenta Crop Protection AG v. FMC Corp.*, PGR2020-00028, Paper 8, at 9, 17, 37 (PTAB Sept. 15, 2020) (claim directed to controlling vegetation growth using an herbicidally effective amount of a compound selected from a genus alleged to encompass over a billion compounds); *Galderma S.A. v. Medy-Tox, Inc.*, PGR2019-00062, Paper 14, at 5 (PTAB Mar. 19, 2020) (claims directed to a method of treatment using a composition that "exhibits a longer lasting effect" compared to other compositions); *Collegium Pharm., Inc. v. Pharma*, PGR2018-00048, Paper 58, at 32, 34 (PTAB Nov. 19, 2021) (claims directed to certain abuse-deterrent dosage forms that provide a therapeutic effect for about 12 or more hours); *Advanced Accelerator Applications USA, Inc. v. Molecular Insight Pharms., Inc.*, PGR2021-00048, Paper 7, at 25 (PTAB July 29, 2021) (claims directed to methods of treatment using compounds having a certain therapeutic efficacy). The written description analysis in these cases concerned whether the

specification adequately described compounds or compositions (beyond any compounds or compositions exemplified in the specification) that would provide the claimed functionality. *See, e.g.*, *Syngenta*, Paper 8, at 39–40; *Collegium*, Paper 58, at 34; *Galderma*, Paper 14, at 18–19; *Advanced Accelerator*, Paper 7, at 25.

The challenged claims are not analogous to the claims in these other cases because the claims here are not directed to "antibodies themselves that have any particular effect (*e.g.*, improving safety)." Prelim. Resp. 49–50. The claims do require an effect—namely, improving the safety of natalizumab treatments—but the claims do not recite that it is the antibodies themselves that improve the safety. Pet. 43. Thus, Petitioner has not demonstrated that these prior Board cases are instructive here.

Petitioner attempts to bolster its argument about lack of possession of the claimed method by arguing that reliable tests for detecting JCV antibodies were not "well-known in the art." Pet. 44. Petitioner asserts that the available tests "struggled to conclusively determine a positive or negative JCV antibody result for at least some patient serum samples." *Id.* (citing, e.g., Ex. 1002 ¶¶ 29, 98–100). Petitioner also asserts that "the '845 Patent specification fails to provide any guidance regarding which serological techniques could reliably detect seroconversion of JCV antibodies and reduce the occurrence of false-positive or false-negative results." *Id.* Petitioner further asserts that it was not until at least 2012 that Patent Owner first published literature correlating or quantifying JCV antibodies with PML risk and updated the Tysabri label to suggest measuring JCV antibodies in natalizumab-treated patients. *Id.* at 44–46

(citing, e.g., Ex. 1016; Ex. 1017; Ex. 1007, 5; Ex. 1008, 4–5; Ex. 1002 ¶¶ 85–87, 102).

These arguments are not persuasive. First, Petitioner's arguments about the alleged lack of reliable testing appear to be based on Petitioner's proposed construction of the claim term "seroconversion . . . of JCV antibodies" as "requir[ing] obtaining a reliable 'positive' result from a serologic test that excludes false positives." Pet. 32. As discussed above in Section II.A, we reject Petitioner's proposed construction. Second, even assuming Petitioner is correct regarding a lack of reliable tests for detecting JCV antibodies, this goes to whether the specification adequately enables the claimed method, not whether it adequately describes it. *See Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1191 (Fed. Cir. 2014) ("[W]ritten description is about whether the skilled reader of the patent disclosure can recognize that what was claimed corresponds to what was described; it is not about whether the patentee has proven to the skilled reader that the invention works, or how to make it work, which is an enablement issue."). The Petition is based on an alleged lack of written description support, not an alleged lack of enablement. *See generally* Pet.; Pet. Reply 1 (acknowledging that enablement is "a ground Petitioner did not advance").

c) Alleged Lack of Support to Show that Monitoring Increasing Titer of JCV Antibodies Can Improve the Safety of Natalizumab Treatment

Petitioner contends that "[t]he challenged claims also lack written description support that monitoring *increasing titer* of JCV antibodies in the serum can improve the safety of natalizumab treatment." Pet. 47. As support, Petitioner argues that "[t]he specification does not cite any data or studies establishing that JCV serum antibodies increased over time in PML

patients or patients treated with natalizumab." *Id.* This argument is not persuasive, because again, such data and studies are not required. *See Ariad*, 598 F.3d at 1352. Additionally, as discussed above in Section II.C.2.a, the priority applications expressly "disclose that monitoring for seroconversion or increasing titer of anti-JCV antibodies, and discontinuing treatment with natalizumab when it is detected, improves the safety of the treatment." Prelim. Resp. 35; Ex. 1025 ¶¶ 15–16, 130; Ex. 1001, 3:45–4:8, 28:12–27. In view of at least these disclosures, Petitioner has not persuaded us that the priority applications lack adequate description that monitoring increasing titer of JCV antibodies can improve the safety of natalizumab treatment.

Petitioner also contends that the specification "does not disclose how to measure increases in JCV antibody levels," including "how often or when serum samples should be taken," "what serological test should be used," and "what increased JCV antibody levels are correlated with a greater risk of PML." Pet. 48 (citing, e.g., Ex. 1002 ¶¶ 104–06). These arguments are unavailing because they concern "how to make [the invention] work," which "is an enablement issue," and Petitioner did not raise an enablement challenge. *Alcon Research Ltd.*, 745 F.3d at 1191; *see also* Prelim. Resp. 53–55; Pet. Reply 1; *see generally* Pet.

d) Alleged Lack of Support for the Claimed Genus of JCV Antibodies

Petitioner asserts that "[c]laim 1 of the '845 Patent requires monitoring a genus of antibodies that are functionally defined by their ability to bind to JCV," and "[t]o support genus claims of this type, the specification must disclose either 'a representative number of species falling within the scope of the genus or structural features common to the members

of the genus.'" Pet. 49 (quoting *Ariad*, 598 F.3d at 1349–50). Petitioner asserts that the specification does not "disclose a representative number of species because there are *no examples* of monitoring any specific JCV antibodies in the '845 Patent specification" or "any common structural features for the claimed antibodies other than that they should bind to JCV." *Id.* at 50, 51 (citing, e.g., Ex. 1002 ¶ 112). Petitioner also asserts that "[t]he various classes of JCV antibodies have both structural and functional differences that materially affect how JCV serum antibodies are monitored." *Id.* at 53 (citing, e.g., Ex. 1002 ¶¶ 112–14).

Petitioner's arguments are unavailing because they fail to adequately consider both the claimed invention and the state of knowledge regarding JCV antibodies. The claimed subject matter here is materially different than the genus/species cases on which Petitioner relies. *See, e.g.*, Pet. 54 (citing *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, 10 F.4th 1330, 1339–40 (Fed. Cir. 2021); *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1164 (Fed. Cir. 2019); *Baxalta Inc. v. Genentech, Inc.*, No. CV 17-509-TBD, 2022 WL 420479, at *2 (D. Del. Jan. 13, 2022)); *see also id.* at 49–55 (citing additional cases). We agree with Patent Owner that Petitioner's "cases relate to patentees' attempts to claim groups of chemicals or molecules," whereas the challenged claims neither "claim any particular compound's function or structure." Prelim. Resp. 56. This difference matters, because as the Federal Circuit has explained, "the representative-species inquiry is directed to whether the inventor 'has truly invented the genus' as opposed to 'a research plan, leaving it to others to explore the unknown contours of the claimed genus.'" *Ajinomoto Co. v. Int'l Trade Comm'n*, 932 F.3d 1342, 1359 (Fed. Cir. 2019) (quoting *AbbVie Deutschland GmbH & Co., KG v.*

Janssen Biotech, Inc., 759 F.3d 1285, 1300 (Fed. Cir. 2014)). Here, the invention is not purported to be a genus of JCV antibodies, but rather is a method of improving the safety of natalizumab treatment by detecting seroconversion and/or an increasing titer of JCV antibodies. *See, e.g.*, Ex. 1001, 3:42–4:8. As such, the representative-species inquiry is inapposite here.

Furthermore, "the amount of disclosure necessary to satisfy the written description requirement will necessarily vary depending on the context, considering such facts as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, and the predictability of the aspect at issue." *Ajinomoto*, 932 F.3d at 1359 (citations omitted). Here, the specification indicates that JCV antibodies, including in a variety of classes, were known. *See, e.g.*, Ex. 1001, 20:62–67 (discussing seroprevalence of JCV antibodies), 25:2–7 (discussing serologic tests for JCV antibodies); Ex. 1025 ¶¶ 100, 116. Indeed, the specification expressly states that "[a] wide variety of serological tests are available to detect JCV," and "[m]ost techniques will detect all classes of antibody, whereas some assays e.g., RIA, EIA, and IF can be designed to detect one specific class, for example, IgM, IgG, or IgA." Ex. 1001, 25:58–67; Ex. 1025 ¶ 116; *see also* Ex. 1002 ¶ 46 (acknowledging availability of a "wide variety" of assays for JCV antibodies), ¶ 74 ("The production of antibodies against JCV was detected in the blood of PML patients long before 2006." (citing Ex. 1028)). Given that the record indicates a variety of JCV antibodies were known as of the filing of the '628 application, Petitioner has not persuaded us that the specification

lacks sufficient disclosure of JCV antibodies useful to practice the claimed method.

To the extent Petitioner is arguing that the specification should include more information on how to monitor different antibodies in different classes, we are also unpersuaded. Petitioner, for example, asserts that "[t]he various classes of JCV antibodies have both structural and functional differences that materially affect how JCV serum antibodies are monitored," such as with respect to which assay to use with the different types of antibodies. Pet. 53 (citing Ex. 1002 ¶¶ 112–14). These arguments are directed to enablement rather than written description, given that they concern "how to make [the invention] work," which "is an enablement issue." *Alcon Research Ltd.*, 745 F.3d at 1191.

e) Petitioner's Failure to Address a Person of Ordinary Skill in the Art's Understanding of Each Pre-AIA Priority Application as of its Filing Date

There is an additional, independent reason supporting our finding that Petitioner has not sufficiently shown that the '845 patent is eligible for post-grant review. Specifically, we agree with Patent Owner that Petitioner's written description analysis is incomplete because "the Petition fails to address the state of the art as it existed on April 9, 2010, *i.e.*, the date of the '845 Patent's latest pre-AIA priority application." PO Sur-reply 1.

As set forth above in Section II.C, the '845 patent claims priority to three pre-AIA applications, namely the provisional application filed in 2006, the '628 application filed in 2007, and U.S. Application 12/757,305, filed on April 9, 2010 (the "2010 application"). We agree with Patent Owner that to establish the '845 patent's eligibility for post-grant review, Petitioner must demonstrate that the priority applications' respective written descriptions

were insufficient in view of the state of the art as of the filing date of each of these three pre-AIA applications (i.e., as of the 2006, 2007, and 2010 filing dates). Prelim. Resp. 24. "This requires [Petitioner] to establish that at *each* of those times, a [person of ordinary skill in the art] would not have understood, in light of the specification and the then-current state of the art, that [Patent Owner] possessed the claimed invention." *Id.* (citing *Ariad*, 598 F.3d at 1351 ("[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter *as of the filing date*.") (emphasis added); *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005) ("The descriptive text needed to meet [the written description] requirement varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence.")).

We agree with Patent Owner that Petitioner "makes no attempt to engage with this requirement, instead focusing its arguments on the state of the art as it existed in 2006 (the filing date of the '931 Application) and 2007 (the filing date of the '628 application), while ignoring the 2010 application." Prelim. Resp. 24. We also agree with Patent Owner that Petitioner's failure to address the state of the art as of the filing of the 2010 application "is fatal, specifically because the Petition and the declaration repeatedly assert and admit that the field was advancing substantially between 2006 and 2010." *Id.* at 27 (citing Pet. 18–19, 23–25; Ex. 1002 ¶¶ 87, 114).

Petitioner asserts that Patent Owner did not supplement the specification of the 2010 application to reflect advances in the state of the art, and thus such advances are irrelevant, because written description

support must come from the four corners of the specification. Pet. Reply 1. Petitioner's argument fails to grapple with controlling case law, which holds that the state of knowledge is relevant in evaluating sufficiency of written description support in the specification. For example, as Patent Owner correctly notes, "*Ariad* itself establishes that written description is evaluated 'as of the filing date' of the particular application, and that 'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue' are all essential 'for evaluating the adequacy of the disclosure.'" PO Sur-reply 2 (quoting *Ariad*, 598 F.3d at 1351); *see also Capon*, 418 F.3d at 1358 ("The 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge."); *Merck Sharp & Dohme Corp. v. Wyeth LLC*, PGR2017-00016, Paper 9, at 14 (PTAB Oct. 20, 2017) ("Petitioner's failure to address each relevant date bolsters our holding that Petitioner fails to show sufficiently that the '060 patent is post grant review eligible."). The Petition acknowledges the advancing state of the art, but fails to assess the impact of those advancements on the adequacy of the disclosure at the time of filing the 2010 application.

Petitioner's reliance on *Biogen Int'l GMBH v. Mylan Pharms. Inc.*, 18 F.4th 1333, 1343–44 (Fed. Cir. 2021) is unavailing. The *Biogen* court stated that information learned well after the patent application was filed was "of no import to the written-description analysis." *Id.* But the *Biogen* court was only considering the retroactive effect of later-learned information on entitlement to an earlier filing date. *See id.* It was not considering the same issue here, namely, whether information learned in between the filing of an

initial patent application and a later continuation application can impact entitlement to the filing date of the later continuation application. Petitioner has not directed our attention to any controlling case indicating that such intervening information is irrelevant.

Petitioner's suggestion that it "addressed the state of the art in 2010, noting that by then '[Patent Owner] still had not determined whether testing for anti-JCV antibodies could be used to assess the risk of PML'" is unavailing. Pet. Reply 3 (quoting Pet. 16). The cited page of the Petition concerns a background discussion. In connection with its post-grant review eligibility analysis, Petitioner did not specifically address the sufficiency or insufficiency of the written description at each relevant priority date in view of the changing state of the art. *See generally* Pet. 33–55.

3. Conclusion

After considering the evidence and arguments before us, we determine that Petitioner has not established that the challenged claims lack written description support in the pre-AIA applications. For this reason, we find that Petitioner has not sufficiently shown that the '845 patent is eligible for post-grant review. Under these circumstances, we need not address Petitioner's three proposed grounds of unpatentability. *See* Pet. 6.

III. CONCLUSION

For the foregoing reasons, we conclude that the information presented in the Petition does not establish that the '845 patent is eligible for post-grant review. Accordingly, we do not institute a post-grant review of claims 1–16 of the '845 patent.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* and no trial is instituted.

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