

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CHARLES RIVER LABORATORIES, INC.
Petitioner,

v.

SEIKAGAKU CORPORATION,
Patent Owner.

PGR2025-00023
Patent 11,959,109 B2

Before MICHAEL J. FITZPATRICK, JAMES A. WORTH, and
TAWEN CHANG, *Administrative Patent Judges*.

FITZPATRICK, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner, Charles River Laboratories, Inc., filed a Petition (Paper 2 (“Pet.”)) to institute a post grant review of claims 1–10 of U.S. Patent No. 11,959,109 B2 (Ex. 1001, “the ’109 patent”). In response, Patent Owner, Seikagaku Corporation, filed: (1) a Discretionary Denial Brief (Paper 6); (2) a Preliminary Response (Paper 7 (“Prelim. Resp.”)); and (3) a Disclaimer of Claim 10 under 37 C.F.R. § 1.321(a) (Ex. 2001). Petitioner filed an Opposition (Paper 8) to the Discretionary Denial Brief.

In a July 10, 2025, Order, the Acting Director denied Patent Owner’s request for discretionary denial and referred the Petition to the Board. Paper 9.

Institution of a post-grant review requires that “the information presented in the petition filed under section 321, if such information is not rebutted, would demonstrate that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable” or that “the petition raises a novel or unsettled legal question that is important to other patents or patent applications.” 35 U.S.C. § 324(a)–(b). Determining whether to institute has been delegated to the Board. *See* 37 C.F.R. § 42.4(a) (“The Board institutes the trial on behalf of the Director.”).

Upon consideration of the Petition and the Preliminary Response, and for the reasons explained below, we determine that it is more likely than not that at least 1 of the claims challenged in the Petition is unpatentable. Accordingly, we grant the Petition.

Although the Petition requests a post-grant review of claims 1–10 and our Rules state that, “[w]hen instituting post-grant review, the Board will authorize the review to proceed on all of the challenged claims and on all grounds of unpatentability asserted for each claim” (37 C.F.R. § 42.208(a)),

the instituted post-grant review shall be confined to claims 1–9 in light of Patent Owner’s disclaimer of claim 10. *See* 37 C.F.R. § 42.207(e) (“The patent owner may file a statutory disclaimer under 35 U.S.C. [§] 253(a) in compliance with § 1.321(a), disclaiming one or more claims in the patent. No post-grant review will be instituted based on disclaimed claims.”); *see also Vectra Fitness, Inc. v. TNWK Corp.*, 162 F.3d 1379, 1383 (Fed. Cir. 1998) (“This court has interpreted the term ‘considered as part of the original patent’ in [35 U.S.C. §] 253 to mean that the patent is treated as though the disclaimed claims never existed.”).

II. BACKGROUND

A. Real Parties in Interest

Each party identifies itself as the sole real party in interest. Pet. 6; Paper 3, 1.

B. Related Matters

The parties direct us to the related applications data referenced in the ’109 patent. Pet. 6–7; Paper 3, 1. The only proceeding identified by either party is IPR2025-00440 involving related U.S. Patent No. 11,236,318 B2 (“the ’318 patent”). Paper 3, 1. The ’109 patent issued from an application which was a continuation of the application from which the ’318 patent issued. Ex. 1001, 1:8–11.

C. The ’109 Patent

The ’109 patent is titled “Recombinant Factor C and Method for Producing the Same, and Method for Measuring Endotoxin.” Ex. 1001, code (54).

Endotoxin is a pyrogen produced by Gram-negative bacteria, and “even a very small amount of endotoxin causes various pathological conditions via bacterial infection.” *Id.* at 1:38–42. “Therefore, detection of endotoxin is essential in pharmaceutical products such as an injection, water, medical devices, and the like.” *Id.* at 1:45–47.

It has long been known that horseshoe crabs naturally undergo blood clotting when infected with endotoxin. *Id.* at 1:52–54. The blood clotting reaction is a cascade that involves three serine protease zymogens and one clottable protein (coagulogen). Ex. 1003 ¶32. Petitioner’s declarant, Siddhartha Jain, Ph.D., explains the reaction as follows:

Endotoxin initiates the cascade by binding to and activating the first serine protease called Factor C. Factor C then cleaves and activates Factor B, which in turn converts pro-clotting enzyme to clotting enzyme. Clotting enzyme cleaves coagulogen, which subsequently forms coagulin gel, giving rise to clotting.

Id. ¶32 (citing Ex. 1001, 1:66–2:11, 13:36–49, Fig. 1).

It was further known that the blood (or hemolymph) of horseshoe crabs could be harvested and employed for the detection of endotoxin in pharmaceutical and medical applications. Ex. 1001, 1:54–56. “However, for using such a lysate, or Factor C, Factor B, and Pro-clotting enzyme purified from the lysate, horseshoe crabs must be caught and blood must be recovered therefrom.” *Id.* at 2:26–29. “Hence, from the viewpoint of protection of biological resources, difficulty is encountered in supply of such ingredients in an inexhaustible manner.” *Id.* at 2:29–31. Thus, there had been a demand for ways to produce the zymogen proteins through genetic

engineering. *Id.* at 2:32–34. According to the ’109 patent, those efforts had not been satisfactory. The ’109 patent explains:

For example, there is known a case where Factor C, Factor B, and Pro-clotting enzyme were expressed in insect cells as host cells, to thereby reconstitute a cascade reaction system (Patent Documents 1 and 2). However, it has been reported that since the reconstituted system contains sodium chloride, magnesium sulfate, or calcium chloride in the reaction system, the cascade reaction is suppressed (Patent Document 1).

Alternatively, there is known a case of using mammalian cells as host cells, wherein Factor C derived from the Singaporean horseshoe crab (*Carcinoscorpius rotundicauda*) was expressed in COS-1, which is a cell line derived from African green monkey kidney cells, as host cells. However, it has been reported that when COS-1 was used as a host, the expressed Factor C was insoluble (Non-Patent Documents 3 and 4). That is, there has never been known a case where functional Factor C is produced using mammalian cells as host cells.

Id. at 2:36–53.

As further background, there are four species of horseshoe crab: *Limulus polyphemus* (American horseshoe crab), *Tachypleus tridentatus* (Japanese horseshoe crab), *Tachypleus gigas* (Southeast Asian horseshoe crab), and *Tachypleus rotundicauda* (also called *Carcinoscorpius rotundicauda* whose common name is Singaporean horseshoe crab). *Id.* at 13:58–62; Ex. 1015 ¶4. According to Dr. Jain, and as relevant to Petitioner’s grounds of unpatentability, although “[t]he gene and amino acid sequences of Factor C proteins from certain species of horseshoe crab . . . were known prior to the earliest claimed priority date of the ’109 patent, . . . the sequences encoding Factor C, Factor B, and Pro-clotting enzyme for the horseshoe crab species *Limulus polyphemus* had **not** been described or fully characterized until much more recently.” Ex. 1003 ¶37.

The '109 patent issued from application number 18/346,420 (“the '420 application”), which was filed July 3, 2023. Ex. 1001, codes (21), (22). The '420 application (and thus the '109 patent) claims priority to numerous related applications, stating:

This is a Continuation of U.S. patent application Ser. No. 17/554,128 filed Dec. 17, 2021, which is a Continuation of U.S. patent application Ser. No. 16/399,386 filed Apr. 30, 2019, now U.S. Pat. No. 11,236,318 [(i.e., the '318 patent challenged in IPR2025-00440)], which is a Continuation of U.S. patent application Ser. No. 15/983,725 [(“the '725 application”)] filed May 18, 2018, now U.S. Pat. No. 10,982,202, which is a continuation of U.S. patent application Ser. No. 14/650,767 [(“the '767 application”)] filed Jun. 9, 2015, now U.S. Pat. No. 10,144,923, which is National Stage of International Application No. PCT/JP2013/083082 filed Dec. 10, 2013, claiming priority based on Japanese Patent Application No. 2012-269840 filed Dec. 10, 2012, the contents of all of which are incorporated herein by reference in their entirety.

Id. at 1:8–21; *see also id.* at code (63).

As explained below, the parties' priority arguments focus exclusively on whether the challenged claims are enabled and described by the '767 application as of the December 10, 2013, international filing date under the Patent Cooperation Treaty.

D. Challenged Claims

The Petition challenges all ten claims of the '109 patent. Of these, only claims 1 and 10 are independent. As stated above, however, claim 10 was disclaimed by Patent Owner after the Petition was filed. Ex. 2001. Each of claims 2–9 depends from claim 1. Ex. 1001, 47:17–48:54. Claim 1 is representative and reproduced below, with Petitioner's bracketed labels preserved.

1. A method for producing an endotoxin assay agent comprising a horseshoe crab Factor C, a horseshoe crab Factor B, and a horseshoe crab Pro-clotting enzyme, the method comprising:

[1A] expressing the horseshoe crab Factor C in a Chinese Hamster Ovary cell or a Human Embryonic Kidney cell as a host cell,

[1B] secreting the horseshoe crab Factor C into an extracellular culture supernatant, and

[1C] recovering the horseshoe crab Factor C in the culture supernatant,

[1D] wherein the recovered horseshoe Factor C has activity of Factor C, and

[1E] wherein the horseshoe crab Factor C is a *Tachypleus tridentatus* Factor C or a *Limulus polyphemus* Factor C,

[1F] expressing the horseshoe crab Factor B having activity of Factor B in a mammalian cell as a host cell,

[1G] expressing the horseshoe crab Pro-clotting enzyme in a mammalian cell as a host cell, and

[1H] producing an endotoxin assay agent comprising the horseshoe crab Factor C, the horseshoe crab Factor B and the horseshoe crab Pro-clotting enzyme,

[1I] wherein the host cell for expressing the horseshoe crab Factor C, the host cell for expressing the horseshoe crab Factor B, and the host cell for expressing the horseshoe crab Pro-clotting enzyme may be the same or different.

Ex. 1001, 47:17–40; *see also* Pet. 61–70 (parsing claim 1 and adding bracketed labels).

E. Post-Grant Review Eligibility

As a threshold issue, we must determine whether the '109 patent is eligible for post-grant review. There are two requirements that must be met for post-grant review to be available.

First, post-grant review is only available if the petition is filed within nine months of the issuance of the challenged patent. 35 U.S.C. § 321(c). Here, the Petition was filed on January 15, 2025, which is just within nine months of the '109 patent's April 16, 2024, issue date. Paper 5, 1; Ex. 1001, code (45).

Second, post-grant review is available only for patents “described in section 3(n)(1)” of the Leahy–Smith America Invents Act (“AIA”), Pub L. No. 112–29, 125 Stat. 284 (2011). *See* AIA § 6(f)(2)(A) (stating that the post-grant review statutes (i.e., 35 U.S.C. §§ 321–329) apply only to patents described in AIA § 3(n)(1)). Such PGR-eligible patents are those that issue from applications that contained, at any time, either (A) a claim having an effective filing date on or after March 16, 2013, or (B) a reference under 35 U.S.C. §§ 120, 121, or 365(c) to such an application. AIA § 3(n)(1)(A)–(B).

With respect to AIA § 3(n)(1)(A), Petitioner contends that the '109 patent is eligible for post-grant review because none of the challenged claims is entitled to an effective filing date earlier than the December 10, 2013. Pet. 9–10; *see also id.* at 23–60 (providing arguments and evidence in support of the contention). Alternatively, with respect to AIA § 3(n)(1)(B), Petitioner points out that Patent Owner filed a “Statement Under 37 C.F.R. § 1.55 or § 1.78 for AIA (First Inventor to File) Transition Applications,” in which it conceded that the '725 application “contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.” Ex. 1022; Pet. 9 (citing Ex. 1022). The '109 patent

claims priority to the '725 application. Ex. 1001, 11–14. Thus, Petitioner has shown that the '109 patent is eligible for post-grant review pursuant to at least AIA § 3(n)(1)(B).

F. Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability:

Claim(s) Challenged	35 U.S.C. §¹	Reference(s)/Basis
1–10	112	Written Description
1–10	112	Enablement
1–10	102	'629 publication ²

III. LEVEL OF ORDINARY SKILL IN THE ART

Petitioner contends a person of ordinary skill in the art (“POSITA”) would have a Ph.D. degree in biological, chemical or biochemical engineering, molecular biology, or biochemistry and at least two years of experience in the field of utilizing or assessing horseshoe crab zymogen proteins (lysate, purified native and/or recombinantly produced) for endotoxin detection and quantitation. More education could substitute for experience to a certain extent, and vice versa.

Pet. 22 (citing Ex. 1003 ¶¶48–49). Patent Owner does not dispute Petitioner’s description of a POSITA in its Preliminary Response. Prelim. Resp. 10.

¹ In addition to other changes to Title 35, the AIA introduced amendments to 35 U.S.C. § 102. Because Patent Owner concedes that the '725 application “contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013” (Ex. 1022), the AIA version of § 102 applies to the '109 patent. AIA § 3(n)(1)(B); Ex. 1001, 1:11–14 (claiming priority to the '725 application).

² US 2019/0241629 A1, published August 8, 2019 (“the '629 publication” (Ex. 1015)).

At this stage, we find Petitioner’s description of the level of ordinary skill in the art sufficiently supported by the record and apply it for purposes of this decision.

IV. CLAIM CONSTRUCTION

In a post-grant review, claim terms “shall be construed using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b), including construing 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.” 37 C.F.R. § 42.200(b).

Neither party proposes an express construction of any claim term. *See* Pet. 22–23; Prelim. Resp. 10.

We determine that no express claim construction is necessary based on the present record.

V. GROUND 1: LACK OF WRITTEN DESCRIPTION

Section 112(a) of Title 35 mandates the following:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

35 U.S.C. § 112(a).³

³ Pursuant to the AIA, § 112 ¶1 was recodified, essentially word for word, at § 112(a). AIA § 4(c)(1). We cite to the AIA version of § 112, which applies “to any patent application that is filed on or after” September 16, 2012 (i.e., one year after the AIA was enacted). *Id.* § 4(e).

In Ground 1, Petitioner contends that claims 1–9 are unpatentable for failing to meet the written description requirement. Pet. 23–38.

As Petitioner points out, “[t]he written description requirement of 35 U.S.C. § 112 exists ‘to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him.’” Pet. 23 (quoting *In re Wertheim*, 541 F.2d 257, 262, (CCPA, 1976)); see also *ICU Med., Inc. v. Alaris Med. Sys.*, 558 F.3d 1368, 1376 (Fed. Cir. 2009) (“[T]he purpose of the written description requirement is to ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor’s contribution to the field of art as described in the patent specification.”). The test for sufficiency of the written description “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.” *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). “[T]he 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.* Whether a specification provides a written description of the claimed invention is a question of fact. *Id.*

Citing *Ariad*, Petitioner argues that, “to assess the written description support of claims such as those challenged herein which were sought in an application filed in 2023 but claim a priority date of a 2012 JP Priority Application and a PCT filing on December 10, 2013, the question is whether a POSA would understand the inventors to have been in possession of the full scope of such claims *in 2013*.” Pet. 23–24 (emphasis added). This argument conflates written description support as required by § 112 with

written description support in a priority application as required by § 120 to benefit from an earlier filing date.

To show that the claims of the '109 patent are unpatentable for lack of written description, Petitioner would have needed to show that the specification as filed (i.e., the '420 application) fails to reasonably convey to those skilled in the art that Patent Owner had possession of the claimed subject matter as of the July 3, 2023, filing date. Petitioner did not. Pet. 23–24. Nor does Petitioner's declarant offer testimony that could support such a showing. See Ex. 1003 ¶50 ("I have been asked to provide my opinions as to the state of the art in this field for purposes of determining what the inventors disclosed as their invention as of December 10, 2013."), ¶51 ("Whenever I offer an opinion in this declaration about the knowledge of a POSA, the manner in which a POSA would have understood the claims of the '109 patent or its description, the manner in which a POSA would have understood the prior art, or what a POSA would have been led to do based on the prior art, I am referencing the December 10, 2013 timeframe.").

Although the '420 application is essentially identical to the '767 application, the person of ordinary skill in 2013 is not the same as in 2023. See *Ariad*, 598 F.3d at 1351 ("[T]he [written description] test requires an objective inquiry into the four corners of the specification *from the perspective of a person of ordinary skill in the art.*" (emphasis added)). Thus, the information presented in the Petition, which is limited to the perspective of a 2013 POSITA, does not demonstrate that it is more likely than not that at least 1 of the claims challenged in the Petition is unpatentable for lack of written description.

VI. GROUND 2: LACK OF ENABLEMENT

In Ground 2, Petitioner contends that claims 1–9 are unpatentable for failing to meet the enablement requirement. Pet. 38–60.

The enablement requirement, like the written description requirement, is set forth in 35 U.S.C. § 112(a). As Petitioner points out, to satisfy the enablement requirement, “the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). To the contrary, “[c]laims are not enabled when, *at the effective filing date of the patent*, one of ordinary skill in the art could not practice their full scope without undue experimentation.” *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013) (emphasis added).

“Enablement is a question of law based on underlying factual findings.” *FS.com Inc. v. Int’l Trade Comm’n*, 65 F.4th 1373, 1376 (Fed. Cir. 2023). As summarized in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), the underlying factual inquiries may “include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” 858 F.2d at 737. These so-called *Wands* factors are not a mandatory or exclusive list of factors to be considered. *Id.*

In making its case, including addressing the *Wands* factors, Petitioner focuses on whether the ’767 application would have enabled a 2013 POSITA to practice the invention. For example, in addressing *Wands* Factors 4, 5, and 7, Petitioner argues that, “while recombinant technology

was not new as of 2013, a significant amount of research and experimentation was required to generate a particular protein, with the ability to detect endotoxin, across a number of different expression systems.” Pet. 42–43; *see id.* at 43 (“[A]s of December 10, 2013, there had been no reports of successful recombinant production of Factors B or Pro-clotting enzyme for any species of horseshoe crab, in any mammalian expression system.”). Likewise, Petitioner’s declarant offers testimony that explicitly does not account for any developments in the art after 2013. *See* Ex. 1003 ¶¶50–51; *see also id.* ¶86 (“In my opinion, the ’767 Application does not provide enough information for a POSA in 2013 to make and use the full scope of challenged claim 1.”).

The information presented in the Petition, which is limited to the perspective of a 2013 POSITA, does not demonstrate that it is more likely than not that at least 1 of the claims challenged in the Petition is unpatentable for lack of enablement.

VII. GROUND 3: ANTICIPATION BY THE ’629 PUBLICATION

Petitioner contends that claims 1–9 are anticipated by the ’629 publication. Pet. 60–86. The ’629 publication is a United States patent application owned by Patent Owner that was published on August 8, 2019. Ex. 1015, codes (43), (73). It is titled “Recombinant Proteins Derived From Genus *Limulus*, and DNA Molecules Encoding Same.” *Id.* at code (54). Two of its three named inventors are also named inventors of the ’109 patent. *Compare id.* at code (72), with Ex. 1001, code (72). Petitioner asserts the ’629 publication as prior art under 35 U.S.C. § 102(a)(1) based on its August 8, 2019, publication date predating the actual filing date of the ’109 patent (July 3, 2023). Pet. 60.

Patent Owner, for its part, does not dispute Petitioner's mapping of the disclosure of the '629 publication to the claims. Prelim. Resp. 56. Rather, Patent Owner asserts that "[t]he Challenged Claims are presumptively entitled to at least a December 10, 2013 priority date." *Id.* But Patent Owner is mistaken on that point of law. See *In re NTP, Inc.*, 654 F.3d 1268, 1276 (Fed. Cir. 2011) ("[A] patent's claims are not entitled to an earlier priority date because the patentee claims priority. . . . Rather, for a patent's claims to be entitled to an earlier priority date, the patentee must demonstrate that the claims meet the requirements of 35 U.S.C. § 120.>").

For example, the Federal Circuit, in an appeal from a civil action, previously explained the following:

At that point TLC [(patent owner)] has the burden of going forward with evidence either that the prior art does not actually anticipate, or, as was attempted in this case, that it is not prior art because the asserted claim is entitled to the benefit of a filing date prior to the alleged prior art. This requires TLC to show not only the existence of the earlier application, but why the written description in the earlier application supports the claim. In the context of the allegedly anticipating Elantec prior art, that means producing sufficient evidence and argument to show that an ancestor to the '250 patent, with a filing date prior to the Elantec date, contains a written description that supports all the limitations of claim 33, the claim being asserted.

Assuming then that TLC's evidence and argument in support of the earlier filing date is now before the court, the burden of going forward again shifts to the proponent of the invalidity defense, Gennum, to convince the court that TLC is not entitled to the benefit of the earlier filing date. "Convince" is the operative word, because if the court is not persuaded by clear and convincing evidence that Gennum is correct, Gennum has

failed to carry its ultimate burden of persuasion, and its defense of invalidity, based on anticipation by the Elantec art, fails.

Tech. Licensing Corp. v. Videotek, Inc., 545 F.3d 1316, 1327–28 (Fed. Cir. 2008). Notably, the Federal Circuit explicitly followed *Technology Licensing* in the IPR context, holding that the same burdens of production apply but that a petitioner’s burden of persuasion of unpatentability is the lower, preponderance standard. See *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1375–76 (Fed. Cir. 2016) (citing *Technology Licensing* and holding that, in an IPR, “a patent challenger has the burden of producing evidence to support a conclusion of unpatentability under § 102 or § 103, but a patentee bears the burden of establishing that its claimed invention is entitled to an earlier priority date than an asserted prior art reference”). Similarly, the Court in *Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1379 (Fed. Cir. 2015), explained the burden shifting as follows:

In this case, Dynamic, as the petitioner, had the burden of persuasion to prove unpatentability by a preponderance of the evidence, and this burden never shifted. Dynamic also had the initial burden of production, and it satisfied that burden by arguing that Raymond anticipated the asserted claims of the ’196 patent under § 102(e)(2).

The burden of production then shifted to National Graphics to argue or produce evidence that either Raymond does not actually anticipate, or, as was argued in this case, that Raymond is not prior art because the asserted claims in the ’196 patent are entitled to the benefit of a filing date (constructive or otherwise) prior to the filing date of Raymond.

Dynamic Drinkware, 800 F.3d at 1379–80.

Although the instant Petition is for a PGR, not an IPR, the same burden shifting framework applies.

Accordingly, we now turn to whether the parties have met their respective burdens of production.

A. Petitioner's Mapping of the '629 Publication to Claim 1

The Petition maps the teachings of the '629 publication to each of claims 1–9. In the Preliminary Response, Patent Owner does not dispute Petitioner's arguments or evidence as to whether the '629 publication teaches the claimed inventions of claims 1–9. Prelim. Resp. 56.

Below, we provide our initial assessment of Petitioner's anticipation arguments for claim 1.

- i. A method for producing an endotoxin assay agent comprising a horseshoe crab Factor C, a horseshoe crab Factor B, and a horseshoe crab Pro-clotting enzyme, the method comprising:*

Although a claim's preamble is not necessarily limiting, Petitioner presents evidence that the '629 publication discloses the subject matter recited in the preamble of claim 1. In that regard, Petitioner cites to numerous paragraphs and claims of the '629 publication and to testimony of Dr. Jain interpreting the '629 publication. Pet. 61–62 (citing Ex. 1015 ¶¶135–137, 169–171, 182–184, 268–277, 350–358, claims 1–4; Ex. 1003 ¶¶146–147).

Petitioner cites disclosures, including a description of the “transfection of the expression plasmids [for three serine protease zymogens] into cells and collection of the recombinant proteins.” Ex. 1015 ¶351; *see also id.* ¶352 (stating that recombinant proteins have the activity of Factor C, Factor B, and Pro-clotting enzyme). Petitioner also cites a description of producing an endotoxin assay agent using the recombinant proteins. *See, e.g., id.* ¶355 (“[B]y utilizing these recombinant proteins, an endotoxin can be detected.”).

Petitioner has shown that it is more likely than not that the '629 publication teaches the preamble of claim 1.

- ii. *[1A] expressing the horseshoe crab Factor C in a Chinese Hamster Ovary cell or a Human Embryonic Kidney cell as a host cell*

For this limitation, Petitioner directs us to, among other things, the '629 publication's disclosure of "using these expression plasmids and the expression plasmid (in which the cDNA of SEQ ID NO: 1 was integrated) obtained in the above ([step] 3-7), and ExpiCHO™ Expression System (Thermo Fisher Scientific), recombinant proteins thereof were obtained as culture supernatant fractions." Ex. 1015 ¶350 (quoted at Pet. 63). In the '629 publication, SEQ ID NO: 1 is the base sequence of cDNA for Factor C. *Id.* ¶¶28–32, 367. And, ThermoFisher Scientific's ExpiCHO™ Expression System uses a Chinese Hamster Ovary ("CHO") cell line. Ex. 1041, 4.

Petitioner has shown that it is more likely than not that the '629 publication teaches limitation [1A].

- iii. *[1B] secreting the horseshoe crab Factor C into an extracellular culture supernatant, and [1C] recovering the horseshoe crab Factor C in the culture supernatant*

For these limitations, Petitioner directs us to, among other things, the '629 publication's disclosure that the "recombinant proteins . . . were obtained as culture supernatant fractions." Ex. 1015 ¶350 (quoted at Pet. 64); *see also id.* ¶352 (describing "the expression and acquisition of the protein (SEQ ID NO: 2) that may have the factor C activity of *Limulus polyphemus*"). In the '629 publication, SEQ ID NO: 2 is the amino acid sequence of Factor C. *Id.* ¶¶28–32, 368.

Petitioner has shown that it is more likely than not that the '629 publication teaches limitations [1B] and [1C].

- iv. *[1D] wherein the recovered horseshoe Factor C has activity of Factor C, and [1E] wherein the horseshoe crab Factor C is a Tachypleus tridentatus Factor C or a Limulus polyphemus Factor C*

For these limitations, Petitioner first directs us to the '629 publication's disclosure that "the expression and acquisition of the protein (SEQ ID NO: 2) that may have the factor C activity of Limulus polyphemus . . . [was] achieved for the first time." Pet. 65 (quoting Ex. 1015 ¶352) (alterations in original). And, as pointed out by Petitioner, the '629 publication describes having confirmed that the recombinant proteins, including the recombinant Factor C, were active.

[I]t was shown for the first time that the expressed protein that may have the factor C activity, the expressed protein that may have the factor B activity, and the expressed protein that may have the proclotting enzyme activity have the factor C activity, the factor B activity, and the proclotting enzyme activity, respectively, and the cascade reaction is caused by contact with an endotoxin. Further, it was shown for the first time that by utilizing these recombinant proteins, an endotoxin can be detected.

Ex. 1015, ¶355 (quoted at Pet. 65–66).

Petitioner has shown that it is more likely than not that the '629 publication teaches limitations [1D] and [1E].

- v. *[1F] expressing the horseshoe crab Factor B having activity of Factor B in a mammalian cell as a host cell*

For this limitation, Petitioner directs us to the '629 publication's description of the "[a]cquisition of cDNA (Second cDNA) of Protein Having

Factor B Activity of *Limulus polyphemus*.” Ex. 1015 ¶¶346–347 (cited at Pet. 67). As Petitioner points out, the cDNA for Factor B was then expressed in a CHO cell line. Pet. 67 (citing Ex. 1015 ¶350). Further, the ’629 publication reports successful acquisition of the recombinant Factor B and confirmation of its activity. Ex. 1015 ¶¶351–355 (cited at Pet. 67).

Petitioner has shown that it is more likely than not that the ’629 publication teaches limitation [1F].

vi. *[1G] expressing the horseshoe crab Pro-clotting enzyme in a mammalian cell as a host cell*

For this limitation, Petitioner directs us to the ’629 publication’s description of the “[a]cquisition of cDNA (Third cDNA) of Protein Having Proclotting Enzyme Activity of *Limulus polyphemus*.” Ex. 1015 ¶¶348–349 (cited at Pet. 68). As Petitioner points out, the cDNA for Pro-clotting enzyme was then expressed in a CHO cell line. Pet. 68 (citing Ex. 1015 ¶350). Further, the ’629 publication reports successful acquisition of the recombinant Pro-clotting enzyme and confirmation of its activity. Ex. 1015 ¶¶351–355 (cited at Pet. 68).

Petitioner has shown that it is more likely than not that the ’629 publication teaches limitation [1G].

vii. *[1H] producing an endotoxin assay agent comprising the horseshoe crab Factor C, the horseshoe crab Factor B and the horseshoe crab Pro-clotting enzyme*

For this limitation, Petitioner directs us to, among other things, the ’629 publication’s statement that, “by utilizing these recombinant proteins, an endotoxin can be detected.” Ex. 1015 ¶355 (quoted at Pet. 69–70).

Petitioner has shown that it is more likely than not that the ’629 publication teaches limitation [1H].

- viii. *[1I] wherein the host cell for expressing the horseshoe crab Factor C, the host cell for expressing the horseshoe crab Factor B, and the host cell for expressing the horseshoe crab Pro-clotting enzyme may be the same or different.*

Petitioner directs us to the '629 publication's teaching of expressing all three of the recombinant proteins in mammals. Petitioner does not explicitly argue whether, in the '629 publication, the host cell for the three recombinant proteins could be the same. However, it is clear enough that it teaches using different host cells. See Ex. 1015 ¶350 (describing expression of recombinant Pro-clotting enzyme in unspecified "mammalian cells," expression of recombinant factor B "according to a literature (Kobayashi et al., 2015, J Biol Chem, 290: 19379-19386 [(i.e., Ex. 1007)])," and describing the use of ThermoFisher Scientific's ExpiCHO™ Expression System); Ex. 1007 (describing expression of recombinant factor B in human embryonic kidney (HEK) cell lines).

Petitioner has shown that it is more likely than not that the '629 publication teaches limitation [1I].

ix. *Conclusion as to Claim 1*

Petitioner has satisfied its burden of production in showing that the '629 publication anticipates claim 1.

x. *Claims 2–9*

Because, as discussed further below, we decide to grant post-grant review of claim 1, we do the same for claims 2–9 and need not separately address the merits as to these dependent claims. See 37 C.F.R. § 42.208(a) ("When instituting post-grant review, the Board will authorize the review to proceed on all of the challenged claims and on all grounds of unpatentability asserted for each claim."); see also *SAS Institute, Inc. v. Iancu*, 584 U.S. 357,

365 (2018) (interpreting the analogous institution statute subsection for *inter partes* reviews (i.e., § 314(a)) to mean that “[o]nce th[e] single claim threshold is satisfied, it doesn’t matter whether the petitioner is likely to prevail on any *additional* claims”).

B. Whether the ’629 is Prior Art to the Challenged Claims

We now turn to whether the ’629 publication is prior art to the challenged claims. We determine that it likely is.

First, as stated above, the challenged claims are not “presumptively entitled” to the December 10, 2013, priority date as Patent Owner argues (*see* Prelim. Resp. 56), or to any of the other priority dates claimed by the ’109 patent. *See, e.g., In re Magnum Oil Tools*, 829 F.3d at 1375–76 (discussed above).

Second, for reasons explained below, Patent Owner’s arguments that the ’767 application provides adequate written description and enablement of the challenged claims as of December 10, 2013—which arguments were presented in opposition to Grounds 1 and 2—are insufficient to show entitlement to an earlier priority date when considered together with Petitioner’s arguments to the contrary. Prelim. Resp. 10–56.

Some of Petitioner’s arguments for lack of written description and enablement are premised on characterizing claim 1 as covering a genus encompassing 3,456 species. *See* Pet. 2, 25–29, 33 (regarding alleged lack of written description), 3, 40–43, 53–54 (regarding alleged lack of enablement). Petitioner arrives at this number by multiplying what it considers to be the number of variations possible for each limitation of claim 1. *Id.* at 28. Petitioner provides a table explaining its calculations, which we reproduce below.

Challenged Claims 1 and 10				
	Expression System	Horseshoe Crab Species	Recovery	Options
Factor B	“Mammalian” (could include), at least: ⁷ • CHO DG44 • CHO K1 • HEK293	• <i>Tachypleus tridentatus</i> • <i>Tachypleus gigas</i> • <i>Limulus polyphemus</i> • <i>Carcinoscorpius rotundicauda</i>	• Secreted into extra-cellular culture supernatant • Not secreted (i.e., lyse cells and recover)	At least 24 options
Factor C	• CHO DG44 • CHO K1 • HEK293	• <i>Tachypleus tridentatus</i> • <i>Limulus polyphemus</i>	• Secreted into extra-cellular culture supernatant	At least 6 options
Pro-Clotting Enzyme	“Mammalian” (could include), at least: • CHO DG44 • CHO K1 • HEK293	• <i>Tachypleus tridentatus</i> • <i>Tachypleus gigas</i> • <i>Limulus polyphemus</i> • <i>Carcinoscorpius rotundicauda</i>	• Secreted into extra-cellular culture supernatant • Not secreted (i.e., lyse cells and recover)	At least 24 options
				At least 3,456 possible combinations

Reproduced immediately above is a table from page 28 of the Petition, purporting to show how Petitioner arrives at a claim scope encompassing “3,456 possible combinations.” Pet. 28.

We are not persuaded, at least on the present record, that the purported 3,456 possible combinations are persuasive of a lack of written description or enablement. For example, in the “Recovery” column, Petitioner notes two options for Factor B and Pro-clotting enzyme, which leads to a quadrupling of the purported possible combinations to 3,456. Yet, Petitioner does not show that the ’767 application fails to describe or enable the two

recovery options: (1) secreting a recombinant protein into an extracellular culture supernatant or (2) lysing the expression cells and recovering the protein. Nor does Petitioner show that combining either recovery option with any of the other recited steps would have required undue experimentation.

What strikes us as much more relevant to the priority issue before us is whether any of the specific options recited in the claim (and identified in Petitioner's table) was not adequately described or enabled. And in that regard, a potential problem for Patent Owner is claim 1's inclusion of proteins from the horseshoe crab species of *Limulus polyphemus*. Claim 1 specifies "a *Limulus polyphemus* Factor C" and generally recites "horseshoe crab Factor B [and] Pro-clotting enzyme," which encompasses all four species and thus *Limulus polyphemus*.

This is a potential problem for Patent Owner because, according to Petitioner:

While challenged claim 1 explicitly recites using *Limulus polyphemus* Factor C for the production of recombinant Factor C (and places no species limitation on the recombinant production of Factor B or Pro-clotting enzyme), the '109 patent inventors did not and could not have described an example of these proteins from *Limulus polyphemus* for the claimed assay because the gene and sequence information for Factor C, Factor B, and Pro-clotting enzyme for *Limulus polyphemus* horseshoe crabs was not yet disclosed as of the claimed priority date of the '109 patent.

Pet. 31 (citing Ex. 1003 ¶¶66; Ex. 1011, 36; Ex. 1015 ¶¶4–13). Claim 1 indeed encompasses the expression, secretion, and recovery of Factor C, Factor B, and Pro-clotting enzyme from the *Limulus polyphemus* species of horseshoe crab. Yet, according to Petitioner, "the sequences encoding

Factor C, Factor B, and Pro-clotting enzyme for the horseshoe crab species *Limulus polyphemus* had **not** been described or fully characterized,” as of 2013 (although the corresponding proteins for two other horseshoe crab species had been). *Id.* at 14. Petitioner supports this argument with Patent Owner’s own statements made after 2013 in the ’629 publication. We reproduce the statements from the ’629 publication we consider the most relevant:

[0008] In order to protect horseshoe crabs, there has been an idea that the reagent is prepared by artificially producing proteins in the amoebocyte lysate using a recombinant technique (PTL 1 to PTL 8). Then, by utilizing recombinant proteins, products such as PyroGene (trademark) (Lonza), EndoZyme (trademark) (Hyglos), and PyroSmart (trademark) (Seikagaku Corporation) have been actually launched in the market.

[0009] However, any of these uses recombinant proteins derived from an organism of the genus *Tachypleus*, and there has been no report of a reagent using recombinant proteins derived from *Limulus polyphemus* which has been widely spread as the lysate reagent.

[0010] The reason for this is because proteins involved in a mechanism of occurrence of clotting by an endotoxin and genes thereof in *Limulus polyphemus* have not been completely identified structurally and functionally.

[0011] In the genus *Tachypleus*, for example, with respect to factor C which is one of the proteins involved in the clotting mechanism, a full gene sequence and a full amino acid sequence derived from *Tachypleus tridentatus* have been reported in 1991 (NPL 1), and a full gene sequence and a full amino acid sequence derived from *Tachypleus rotundicauda* (*Carcinoscorpius rotundicauda*) have been reported in 1995 (NPL 2).

[0012] However, in *Limulus polyphemus*, complete identification of these proteins and genes from both structural and functional aspects has not been achieved even though 20

years or more has passed since the reports regarding the genus *Tachypleus* described above were published. This is because accurate determination of the full-length sequence structures and elucidation of the expression and functions of these proteins and genes could not be achieved by general techniques due to various differences in biomolecules, diversities, etc. because of differences in genera or species of horseshoe crabs.

[0013] In fact, as part of the invertebrate genome project using a next-generation sequencer, a comprehensive analysis of genes of *Limulus polyphemus* has been carried out (<http://genome.wustl.edu/genomes/detail/limulus-polyphemus/>), however, the full-length sequences of all proteins and genes involved in the clotting mechanism of *Limulus polyphemus* have not been elucidated yet. This fact also supports the difficulty in accurate determination of the full-length sequence structures of these proteins and genes in *Limulus polyphemus*.

...

[0025] The present inventors were successful in the acquisition of full-length cDNAs encoding all protein factors involved in the clotting mechanism of *Limulus polyphemus* which no one had ever been successful for a long time, and the expression of all recombinant proteins thereof, and further found that these can be utilized in various applications, and thus completed the present invention.

Ex. 1015 ¶¶8–13, 25.

These statements support Petitioner’s argument that the ’767 application lacks a written description and enablement of the full scope of the challenged claims as of 2013, which scope extends to recombinant proteins of the *Limulus polyphemus* species of horseshoe crab.

Patent Owner, for its part, argues that declaration evidence presented in a European Patent Office (“EPO”) proceeding supports its position that the ’767 application fully describes and enables the challenged claims. Prelim. Resp. 27–41. That proceeding is an Opposition against Patent

Owner's EP 3530670 patent ("the '670 Opposition"). *See* Ex. 2006 (Notice of the '670 Opposition). As alleged by Patent Owner, the anonymous Opponent that requested the '670 Opposition filed a declaration by a Michael A. Frohman ("the Frohman Declaration"), which contains testimony that is inconsistent with positions advanced by Petitioner in these proceedings. *See, e.g.*, Prelim. Resp. 27 ("Professor Frohman's opinion that there was ***no reason to believe*** that *L. polyphemus* Factor C would have been difficult to express by following the examples in the '109 Patent (EX2004 ¶¶ 44–47)."). Patent Owner additionally presents evidence tending to show that the anonymous Opponent that requested the '670 Opposition was Petitioner. *See id.* at 28–36.

As an initial matter, the Frohman Declaration was submitted in a different proceeding and in a different forum, yet our rules contemplate objections to admissibility only after institution. *See* 37 C.F.R. § 42.64(b)(1) ("Any objection to evidence submitted during a preliminary proceeding must be filed within ten business days of the institution of the trial."); *compare* Fed. R. Evid. 801(c) (defining hearsay as a statement, not made at the current trial or hearing, "offer[ed] in evidence to prove the truth of the matter asserted"), *with* Fed. R. Evid. 801(d)(2) (excluding from hearsay statement offered against an opposing party where statement was made by "a person whom the party authorized to make a statement on the subject" or by a "party's agent or employee on a matter within the scope of that relationship and while it existed"). However, even if we were to take it into account, the Frohman declaration would not tip the balance of evidence in favor of denying institution.

First, although Patent Owner has identified statements in the Frohman declaration it argues shows "there was ***no reason to believe*** that *L.*

polyphemus Factor C would have been difficult to express by following the examples in the '109 Patent,” Patent Owner has not made a similar showing as to Factor B or Pro-clotting enzyme from *Limulus polyphemus*.

Second, and perhaps most significantly, the record before us contains statements by Patent Owner in its '629 publication that all prior efforts to obtain recombinant cascade proteins from *Limulus polyphemus* had proved fruitless. Ex. 1015 ¶¶8–13, 25.

Accordingly, Patent Owner has not met adequately its burden of production to show that the challenged claims are entitled to a priority date that would obviate the '629 publication as prior art. In the alternative, to the extent Patent Owner may be considered to have met its burden of production, we find Petitioner has nevertheless established it is more likely than not that the challenged claims are not entitled to an earlier priority date based on evidence currently of record and the '629 publication is, therefore, prior art.

VIII. CONCLUSION

For the reasons discussed above, we are persuaded 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).

IX. ORDER

Accordingly, it is:

ORDERED that the Petition is granted and a post-grant review is hereby instituted as to claims 1–9 of U.S. Patent No. 11,959,109 B2; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 324(d) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this decision.

PGR2025-00023
Patent 11,959,109 B2

For PETITIONER:

Scott McKeown
Flora Luo
WOLF, GREENFIELD & SACKS, P.C.
smckeown-ptab@wolfgreenfield.com
fluo-ptab@wolfgreenfield

FOR PATENT OWNER:

Alexander Stein
Christopher Betti
MORGAN, LEWIS & BOCKIUS LLP
alexander.stein@morganlewis.com
christopher.betti@morganlewis.com