

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CHARLES RIVER LABORATORIES, INC.,
Petitioner,

v.

SEIKAGAKU CORPORATION,
Patent Owner.

IPR2025-00440
Patent 11,236,318 B2

Before MICHAEL J. FITZPATRICK, SUSAN L. C. MITCHELL, and
TAWEN CHANG, *Administrative Patent Judges*.

Opinion for the Board filed by Administrative Patent Judge CHANG.

Opinion dissenting filed by Administrative Patent Judge FITZPATRICK.

CHANG, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining Challenged Claim Unpatentable
35 U.S.C. § 318(a)

Denying Patent Owner's Revised Contingent Motion to Amend
35 U.S.C. § 316(d)

I. INTRODUCTION

This is a Final Written Decision in an *inter partes* review challenging the patentability of claim 21 of U.S. Patent No. 11,236,318 B2 (Ex. 1001, “the ’318 patent”). We have jurisdiction under 35 U.S.C. § 6.

Petitioner has the burden of proving unpatentability of the challenged claim by a preponderance of the evidence. 35 U.S.C. § 316(e). Having reviewed the parties’ arguments and cited evidence, for the reasons discussed below, we find Petitioner has demonstrated by a preponderance of the evidence that claim 21 is unpatentable.

A. Procedural History

Petitioner Charles River Laboratories, Inc. filed a Petition requesting *inter partes* review of claim 21 of the ’318 patent. Paper 2 (“Pet.”). Patent Owner, Seikagaku Corporation, timely filed a Discretionary Denial Brief and a Preliminary Response, after which Petitioner filed an Opposition to Patent Owner’s Discretionary Denial Brief. Papers 6–8. The Director denied Patent Owner’s request for discretionary denial and referred the Petition to the Board. In view of the then-available preliminary record, we instituted an *inter partes* review. Paper 14 (“Inst. Dec.”).

Thereafter, Patent Owner filed a Response to the Petition (Paper 26, “PO Resp.”); Petitioner filed a Reply (Paper 32, “Reply”); and Patent Owner filed a Sur-reply (Paper 35, “Sur-reply”). Patent Owner also filed a Contingent Motion to Amend pursuant to 35 U.S.C. § 316(d) (Paper 27), which Petitioner opposed (Paper 33). On March 27, 2026, we issued Preliminary Guidance on Patent Owner’s Motion pursuant to 37 C.F.R. § 42.121(e). Paper 34. Patent Owner subsequently filed a Revised Contingent Motion to Amend (Paper 36, “RMTA”), to which Petitioner filed

an Opposition (Paper 42, “RM TA Opp.”). Patent Owner and Petitioner further filed a Reply (Paper 44, “RM TA Reply”) and a Sur-reply (Paper 47, “RM TA Sur-reply”) in support of, respectively, the Revised Contingent Motion to Amend and the Opposition.

With authorization from the Board, the parties further filed supplemental briefs on the relevance, to this proceeding, of the Federal Circuit’s April 16 decision in *Teva Pharmaceuticals Int’l GmbH v. Eli Lilly & Co.*, 172 F.4th 1367 (Fed. Cir. 2026). Papers 45, 46. An oral hearing for this proceeding was held on June 9, 2026, and the transcript of that hearing is of record. Paper 51 (“Tr.”).

B. Real Parties-in-Interest

Petitioner identifies itself as the real party-in-interest. Pet. ix. Patent Owner identifies itself as the real party-in-interest. Paper 3, 1.

C. Related Matters

Petitioner identifies the applications set forth in the Related U.S. Application Data section of the ’318 patent. Pet. ix; Ex. 1001, code (63). Petitioner further identifies U.S. Patent Application No. 17/554,128, filed December 17, 2021, and U.S. Patent Application No. 18/346,420 (now U.S. Patent No. 11,959,109), filed July 3, 2023, as claiming benefit of priority to the ’318 patent. Pet. ix.

Patent Owner states that the ’318 patent is a “family member patent of U.S. Patent Nos. 11,959,109, 10,982,202, and 10,144,923” and that “[a] continuation application (App. Ser. No. 17,554,128) is pending in the

family.” Paper 3, 1. Patent Owner notes that “Petitioner has challenged U.S. Patent No. 11,959,109 in PGR2025-00023.”¹ *Id.*

D. The ’318 Patent and Relevant Background

The ’318 patent, titled “Recombinant Factor C and Method for Producing the Same, and Method for Measuring Endotoxin,” was filed as U.S. Patent Application No. 16/399,386 (the ’386 application) on April 30, 2019, and claims the benefit of U.S. Patent Application No. 15,983,725 (the ’725 application, now U.S. Patent No. 10,982,202), filed on May 18, 2018, and U.S. Application No. 14/650,767 (the ’767 application, now U.S. Patent No. 10,144,923), filed as Application No. PCT/JP2013/083082 (the ’082 PCT) on December 10, 2013. Ex. 1001, codes (54), (21), (22), (63), 1:8–16.

1. Endotoxin Detection Using Horseshoe Crab Lysate

Endotoxin is a lipopolysaccharide in the outer membrane of Gram-negative bacteria that can cause “various pathological conditions via bacterial infection.” Ex. 1001, 1:27–31. “Therefore, detection of endotoxin is essential in pharmaceutical products such as an injection, water, medical devices, and the like.” *Id.* at 1:34–36.

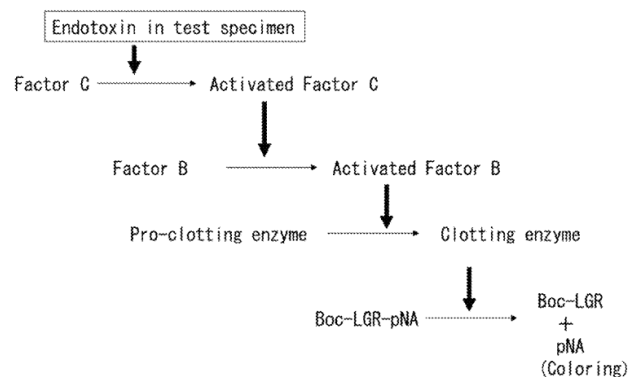
The Specification explains “it has been known that the American horseshoe crab (*Limulus polyphemus*) undergoes blood clotting when it is infected with a Gram-negative bacterium,” and the art has developed a “limulus test” to detect endotoxin by detecting the clotting enzyme or

¹ The Board instituted post-grant review in PGR2025-00023 on September 9, 2025. PGR2025-00023, Paper 14. We are concurrently issuing a Final Written Decision in that proceeding. *Id.*, Paper 43.

measuring the coagulation reaction when an amebocyte² lysate of a horseshoe crab comes into contact with endotoxin. Ex. 1001, 1:40–67, 2:1–9. The Specification further teaches that, in addition to *Limulus polyphemus* (American horseshoe crab), “[e]xamples of the horseshoe crab include *Tachypleus tridentatus* (Japanese horseshoe crab), . . . *Carcinoscorpius rotundicauda* (Southeast Asian (Singaporean) horseshoe crab), and *Tachypleus gigas* (Southeast Asian horseshoe crab).” *Id.* at 13:30–34.

Figure 1 of the ’318 patent, reproduced below, shows the cascade reaction that occurs when endotoxin comes into contact with the horseshoe crab lysate:

[Fig. 1]



Ex. 1001, Fig. 1. Figure 1 depicts “[a] chart showing a cascade reaction system of the limulus test.” *Id.* at 12:15–16. In particular, endotoxin activates Factor C, a serine protease zymogen present in the horseshoe crab lysate, which activates Factor B, which in turn converts the pro-clotting enzyme into the corresponding clotting enzyme, which can “hydrolyze[] a specific site of a coagulogen molecule present in the lysate” to form a

² An amebocyte is a type of cell in the blood (hemolymph) of the horseshoe crab. Ex. 1010, 22.

coagulin gel. *Id.* at 1:55–67. Alternatively, as shown in Figure 1, the presence of the clotting enzyme may be confirmed via its reaction with a detection substrate (Boc-LGR-pNA) to release a dye (pNA). *Id.* at 21:3–11, 24:14–42, Fig. 1.

2. Recombinant Horseshoe Crab Factor C and Residual Activity

The Specification explains that, “from the viewpoint of protection of biological resources,” there is a demand to reconstitute the cascade reaction of the limulus test using genetic engineering instead of using lysate requiring horseshoe crab blood. Ex. 1001, 2:14–22. However, existing recombinant systems using insect and mammalian cells as hosts result in suppression of the cascade reaction due to the presence of certain salts in the reconstituted system, or insoluble and thus non-functional Factor C. *Id.* at 2:24–41.

According to the Specification, therefore, an object of its invention is “to provide a novel recombinant horseshoe crab Factor C, and a method for producing the recombinant Factor C.” Ex. 1001, 2:65–67. Furthermore, because “injections to be administered in vivo generally contain a variety of salts (ions)” and detection of endotoxin is often required during its production, another object of the invention is “to provide a reconstituted cascade reaction system which is not susceptible to reaction inhibition even in the presence of a salt (ion).” *Id.* at 3:1–8.

One measure of the degree to which the cascade reaction is inhibited in the presence of salt is “residual activity,” defined in the ’318 patent as

a relative reactivity (%) observed for a measurement specimen (endotoxin concentration: 0.05 EU/mL) prepared by adding endotoxin to an ion-containing test specimen, with respect to the reactivity observed for another measurement specimen (endotoxin concentration:

0.05 EU/mL) prepared by adding endotoxin to injection water as 100%, in the assay system shown in FIG. 4.

Ex. 1001, 18:8–15. Figure 4 of the Specification is reproduced below:

[Fig. 4]

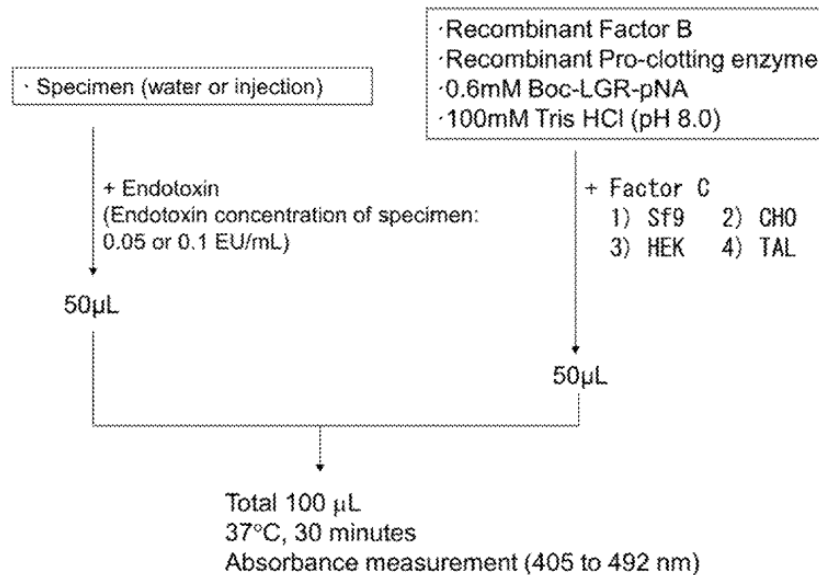


Figure 4 depicts “[a] scheme of measuring the activity of Factor C.”

Ex. 1001, 12:26.

The Specification further states that the inventors

have found that a recombinant horseshoe crab Factor C can be produced by use of human cells or Chinese hamster cells as host cells, and that endotoxin can be measured by use of the thus-produced recombinant Factor C while reaction inhibition in the presence of a salt (ion) is mitigated.

Ex. 1001, 3:12–16.

E. Challenged Claim

Petitioner challenges claim 21 of the '318 patent. The claim is reproduced below:

21. A horseshoe crab Factor C protein having activity of Factor C,
wherein the horseshoe crab is *Limulus polyphemus*,
and wherein the horseshoe crab Factor C protein is produced through being recombinantly expressed from a Human Embryonic Kidney (HEK) 293 cell,
and
wherein the Factor C protein exhibits a residual activity of at least one selected from the group consisting of:
(1) 10% or higher in the presence of 21 mM sodium citrate; and
(2) 15% or higher in the presence of 16 mM magnesium sulfate.

Ex. 1001, 76:50–61 (claim 21).

F. Asserted Grounds of Unpatentability

Ground	Claim(s) Challenged	35 U.S.C § ³	Reference(s)/Basis
1	21	103	Mizumura, ⁴ '498 PCT ⁵

³ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. AIA § 3(b)–(c). Because Patent Owner previously represented that the parent '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. 1011), the AIA versions of §§ 102 and 103 apply to the '318 patent. AIA § 3(n)(1)(B); *see also* Pet. 8 n.2 (pointing out Patent Owner’s representation to the Patent Office).

⁴ Mizumura et al., US 2015/0307864 A1, published Oct. 29, 2015 (Ex. 1009, “Mizumura”).

⁵ Mizumura et al., WO 2018/074498 A1, published April 26, 2018 (Ex. 1005, “'498 PCT”).

Ground	Claim(s) Challenged	35 U.S.C § ³	Reference(s)/Basis
2	21	103	Mizumura, McClymont ⁶

Petitioner relies on supporting evidence including the declarations of Dr. Siddhartha S. Jain. (Ex. 1002, “Jain Declaration” and Ex. 1071, “Second Jain Declaration”). Patent Owner relies on supporting evidence including the declarations of Brian C. Schaefer, Ph.D. (Ex. 2038, “Schaefer Decl.” and Ex. 2108, “Second Schaefer Decl.”) and Tina Morris, Ph.D. (Ex. 2042, “Morris Decl.”).

II. ANALYSIS OF ASSERTED GROUNDS

A. Principles of Law

“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016). The burden of persuasion never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). To prevail, Petitioner must demonstrate unpatentability by a preponderance of the evidence. 35 U.S.C. § 316(e).

However, Patent Owner has the burden of production to show that the claim is entitled to a filing date prior to the date of the alleged prior art. *See Tech Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1327 (Fed. Cir. 2008). Our reviewing court has explained that “[t]he burden of production cannot be met without some combination of citing the relevant record evidence with specificity and explaining the significance of the

⁶ Karen McClymont, Structural Studies of the Endotoxin Sensing Protein Factor C (2017) (Ph. D. dissertation, University of Glasgow) (Ex. 1010, “McClymont”).

produced material in briefs.” *Parus Holdings, Inc. v. Google LLC*, 70 F.4th 1365, 1372 (Fed. Cir. 2023).

Pursuant to 35 U.S.C. § 120, a patent application may be entitled to the filing date of a prior application, but only “for an invention disclosed [in the prior application] in the manner provided by [35 U.S.C. §] 112(a) (other than the requirement to disclose the best mode).” Section 112(a) in turn requires the specification to (1) contain a written description of the claimed invention and (2) enable a skilled artisan to make and use the same without undue experimentation. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1340 (Fed. Cir. 2010) (en banc).

The test for sufficiency of a written description is whether the disclosure “reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.” *Ariad*, 598 F.3d at 1351. That “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.* “[T]he level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology.” *Id.* (citing *Capon v. Eshhar*, 418 F.3d 1349, 1357–58 (Fed. Cir. 2005)).

The test for enablement is whether a person of ordinary skill in the art would be able to practice the claimed invention without “undue experimentation.” *Amgen Inc. v. Sanofi, Aventisub LLC*, 987 F.3d 1080, 1084. Factors to be considered in determining whether undue experimentation is needed 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.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

In general, a claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. *See KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

An obviousness determination based on a combination of teachings requires finding “a motivation to combine accompanied by a reasonable expectation of achieving what is claimed in the patent-at-issue.” *See Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016). “[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *KSR*, 550 U.S. at 419–20.

We address Petitioner’s challenges with these standards in mind, and in view of the definition of the skilled artisan and the claim constructions discussed below.

B. Level of Ordinary Skill in the Art

Relying on the Jain Declaration, Petitioner asserts that “[a] POSA in the technical field relating to the ’318 patent would have a Ph.D. degree in biological, chemical or biochemical engineering, molecular biology, or biochemistry and at least two years of experience utilizing or assessing horseshoe crab Factor C (lysate, purified native and/or recombinantly produced) for endotoxin detection and quantitation.” Pet. 19 (citing Ex. 1002 ¶¶ 61–66). Petitioner asserts that “[m]ore education could substitute for experience, and vice versa.” *Id.* Patent Owner did not dispute Petitioner’s definition of POSA in its Preliminary Response. Paper 7, 13.

In our Institution Decision, we noted that the Jain Declaration, which the Petition cited for support, defined a POSA in the December 10, 2013, timeframe. Inst. Dec. 12. We explained that,

[b]ecause the test of obviousness depends on the effective filing date of the challenged claim, which the parties dispute, December 10, 2013 may not be the appropriate time frame for determining the level of ordinary skill in the art for purposes of determining obviousness, even if it were the appropriate time frame for purposes of determining the effective priority date for claim 21.

Id. Accordingly, based on the then-available preliminary record, we accepted Petitioner’s proposed definition for purposes of our Institution Decision, with the caveat that the level of skill may change with additional evidence submitted at trial. *Id.*

In its Response after institution of trial, Patent Owner asserts that a POSA of “[c]laim 21 does not require knowledge of biological, chemical or biochemical engineering” and proposes instead that such “a POSA would have a Ph.D. in molecular biology, biochemistry, or enzymology and at least two years of experience with cloning genes, expressing cloned genes as

proteins, and characterizing them.” PO Resp. 10 (citing Schaefer Decl. ¶ 49). Patent Owner further asserts that “[t]he POSA may also collaborate with others, including those with specific experience in conducting structure-function analyses of enzyme function, evaluating the activity of horseshoe crab zymogen proteins individually, or in a cascade reaction for endotoxin detection and quantitation.” *Id.* at 11.

Petitioner’s and Patent Owner’s proposed definitions of a POSA overlap to a significant degree, i.e., a person with a Ph.D. in a discipline related to biological sciences and having had at least two years of work experience. However, the parties’ proposals differ slightly in the specific subjects in which a POSA would have had a doctoral degree, and whether the person’s work experience must have been directly related to horseshoe crab Factor C.

As an initial matter, we find that a rigid requirement as to the subject of a POSA’s doctoral degree (*e.g.*, biochemical engineering, enzymology), or experience working specifically with horseshoe crab proteins, is not consistent with the evidence of record. *See, e.g.*, Ex. 1067, 20:23–21:2 (Dr. Schaefer testifying that the fact the “name of [his] Ph.D. is immunology . . . does not change the fact that the core of [his] thesis training was really in molecular biology”), 22:3–15 (explaining “the fact that the production of proteins recombinantly is mostly species agnostic”); Ex. 1069, 45:20–47:17 (Dr. Morris testifying that whether a person is a POSA depends on the person’s “experience, [] publications,” and work done for the Ph.D. rather than the name of the Ph.D. program). We also find that evidence of record supports Petitioner’s assertion that, for purposes of defining a POSA, “[m]ore education could substitute for experience, and vice versa.” *See, e.g.*, Pet. 19; Ex. 1065, 99:14–100:3.

Accordingly, based on the entirety of the trial record, we find a POSA with respect to the claims of the '318 patent would have had a Ph.D. in molecular biology, biochemistry, or a related discipline, and about two years of experience with cloning genes, expressing cloned genes as proteins, and/or characterizing such cloned genes and proteins, with more education being able to substitute for experience, and vice versa. A POSA may also have collaborated with others, including those with specific experience in utilizing or assessing horseshoe crab Factor C for endotoxin detection and quantitation.

C. Claim Construction

The parties agree that “the terms in claim 21 can be afforded their plain and ordinary meaning for purposes of this proceeding” without further construction. Pet. 19–20; PO Resp. 11. Because express claim construction is not needed to resolve the issues in this case, we need not, and do not, construe expressly any claim term for purposes of this Decision. *See Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1375 (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)).

D. Overview of References Asserted Against Claim 21

1. Mizumura (Exhibit 1009)

Mizumura is a United States Patent Application Publication, US 2015/0307864 A1, titled “Novel Recombinant Factor C and Method for Producing the Same, and Method for Measuring Endotoxin,” which was published on October 29, 2015. Ex. 1009, codes (19), (12), (10), (43), (54). Mizumura is the publication of the '767 application, i.e., the application filed

on December 10, 2013, that is the grandparent of the application from which the '318 patent issued. *Id.*, code (21).

2. The '498 PCT (Exhibit 1005)

The '498 PCT is an International Application published under the Patent Cooperation Treaty, WO 2018/074498 A1, titled “Recombinant Proteins Derived from *Limulus* Bacterium, and DNA Molecules Encoding Same,” which was published on April 26, 2018. Ex. 1005, codes (12), (43) (10), (54).

The '498 PCT states that its inventors

have succeeded in obtaining full-length cDNAs encoding all of the protein factors involved in the coagulation mechanism of *Limulus polyphemus*, something that no one had succeeded in doing for many years, and in expressing all of the recombinant proteins, and have further discovered that these can be used for a variety of purposes, thereby completing the present invention.

Ex. 1005 ¶ 17. The '498 PCT discloses examples of such full-length cDNA (SEQ ID NOs: 1, 3) and amino acid (SEQ ID Nos: 2, 4) sequences. *See, e.g., id.* ¶ 173, pp. 49–57. It further discloses a “DNA construct containing [the] cDNA, transformed cell, and method for producing recombinant . . . protein using the same.” *Id.* ¶¶ 20–46, 128–129. With respect to methods for producing recombinant protein, the '498 PCT states that host cells can include “mammalian cells and insect cells” and that “[h]uman cells include human embryonic kidney (HEK) derived cell lines,” an example of which is HEK293. *Id.* ¶ 39.

3. McClymont (Exhibit 1010)

McClymont is a thesis submitted in fulfillment of the requirements for the Degree of Doctor of Philosophy at the University of Glasgow, titled

“Structural studies of the endotoxin sensing protein Factor C,” which was published on April 7, 2017. Ex. 1010, 1, prefatory page.

McClymont states as its aim “to develop a better understanding of how Factor C is activated by endotoxin binding and to identify conformational changes that take place as a result.” Ex. 1010, 2. In particular, “fragments of Factor C protein were produced recombinantly in *Escherichia coli* to determine the structures of the individual domains and identify the endotoxin binding region more precisely,” and “expression of the whole Factor C protein in eukaryotic expression systems was attempted to produce material for experiments that would shed light on any overall conformational change that occurs.” *Id.*

In its Appendix B, McClymont provides the predicted amino acid and DNA sequences of *Limulus polyphemus* Factor C. Ex. 1010, 159 (App. B). McClymont further tested three eukaryotic expression systems for suitability for *Limulus polyphemus* Factor C expression: yeast (*Pichia pastoris*), insect (*Baculovirus* system) and mammalian (Flp-In™ TREx™ system). Ex. 1010, 38.

E. Priority Date of Claim 21

Because Mizumura, the '498 PCT, and McClymont have publication dates earlier than the filing date of the application for the '318 patent, whether these references qualify as prior art depends on the effective filing date of challenged claim 21. Therefore, a threshold issue for analyzing the asserted grounds of unpatentability is the priority date to which claim 21 is entitled.

Patent Owner asserts that claim 21 is entitled at least to an effective filing date of December 10, 2013, the filing date of the '082 PCT. PO

Resp. 13. Petitioner asserts that claim 21 is entitled to an effective filing date of no earlier than April 30, 2019, the actual filing date of the '386 application from which the '318 patent issued. Pet. 20–22.

As noted above, in order to establish priority to the filing date of a prior application, the prior application must (1) contain a written description of the claimed invention and (2) enable a skilled artisan to make and use the same without undue experimentation. 35 U.S.C. § 120; *Ariad*, 598 F.3d at 1340. We discuss these issues below.⁷

1. Written Description

a. Petitioner's Position

Petitioner argues that a POSA would not have reasonably understood the inventors to be in possession, as of December 10, 2013, of a HEK-293 recombinant *L. polyphemus* horseshoe crab Factor C protein with the claimed residual activity, i.e., (1) 10% or higher in the presence of 21 mM sodium citrate or (2) 15% or higher in the presence of 16 mM magnesium sulfate. Pet. 23.

⁷ Although Patent Owner asserts a priority date of at least December 10, 2013, which is the filing date of the '082 PCT, Petitioner analyzes the adequacy of disclosure with respect to the '767 application as “representative” of the '082 PCT. Pet. 22. Petitioner asserts, and Patent Owner has not disputed, that the only difference between the '082 PCT and the '767 application is the addition of a paragraph, relating to the zymogen cascade reaction, that does not materially change the analysis with respect to issues relevant to this proceeding. *Id.* at 21–22. Patent Owner similarly cites to the '767 application in its arguments. PO Resp. 11 (asserting that “the '767 Application provides ample written description support and enables the full scope of claim 21”). Accordingly, we analyze the parties' arguments regarding the effective filing date of claim 21 with reference to the disclosure of the '767 application.

Petitioner asserts that that the '767 application at most discloses experimental protocols for producing HEK-293 recombinant Factor C proteins of the *T. tridentatus* horseshoe crab with residual activity falling within the claimed range. Pet. 23. Petitioner further asserts that, even for that Factor C protein, which is from a different horseshoe crab species, the '767 application discloses data demonstrating only a single residual activity value. *Id.* at 23–24.

Petitioner argues that a POSA would not have expected protocols for producing recombinant Factor C protein for one species of horseshoe crab (*T. tridentatus*) to yield functional recombinant proteins from a ***different*** species of horseshoe crab (*L. polyphemus*), much less that such proteins from the different species would exhibit residual activity in and across the full scope of the claimed ranges. Pet. 24. Petitioner argues that this is particularly the case because the full sequence of *L. polyphemus* Factor C protein was neither publicly available nor described in the '767 application, and evidence suggests differences between the sequences of *L. polyphemus* and *T. tridentatus*. *Id.*

b. Patent Owner's Position

Patent Owner argues that examples are not needed to satisfy the written description requirement and that Petitioner incorrectly analyzes claim 21 as a broad genus claim that requires either a disclosure of representative species or structure features common to the members of the genus, when in fact it narrowly claims Factor C protein from a specific horseshoe crab species recombinantly expressed from a specific host cell, that meets a minimum residual activity threshold in specifically claimed salt solution concentrations. PO Resp. 13, 25; *see also* Sur-reply 6–10.

Patent Owner argues that the '767 application “provides the requisite description such that a POSA would have understood the inventors had possession of the invention of claim 21 as of at least the 2013 filing date for the '767 application.” PO Resp. 13; *see also id.* at 26–27. Patent Owner argues that, in addition, a significant amount of coding sequence information regarding *L. polyphemus* Factor C protein was publicly available and that, based on similarities between the coding sequences of Factor C proteins from different horseshoe crab species and known similarities in the function of such Factor C proteins, a POSA would reasonably have understood the inventors to be in possession of the claimed recombinant Factor C protein, including with respect to the residual activity limitation. *Id.* at 15–19, 22–24, 27. Patent Owner also cites to Petitioner’s arguments in the EP Opposition that, as of 2016, determining the sequence information of a known protein such as *L. polyphemus* Factor C would have been routine, and that a patent document having the same disclosure as in the '767 application “disclosed” recombinant *L. polyphemus* Factor C protein. *Id.* at 29–31.

c. Analysis

On this record, we find Petitioner’s arguments persuasive. We explain our reasoning below.

As an initial matter, we agree with Patent Owner that neither examples nor actual reduction to practice is necessary for adequate written description. PO Resp. 12; *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006). However, as Patent Owner acknowledges, the '767 application must still provide description that reasonably conveys to a POSA that the inventors were in possession of the claimed recombinant Factor C protein. PO Resp. 12–13.

i. Disclosures in the '767 Application

Patent Owner first points to disclosures in the '767 application to argue that an ordinarily skilled artisan would have understood that the inventors had possession of the claimed recombinant *Limulus polyphemus* Factor C protein. These disclosures, some of which are paraphrased, are summarized below:

- Statement in “Modes for carrying out the Invention” that “the ‘Factor C of the present invention is a ***Factor C derived from a horseshoe crab***’” and identification of *Limulus polyphemus* as a known species, PO Resp. 13 (citing Ex. 1006, 40), 26, n.4, 27;
- Statement that “‘Factor C of the present invention’ can be expressed in HEK293 cells” and example that “describes steps to produce Factor C using HEK293 cells as the host cell,” PO Resp. 13–14 (citing Ex. 1006, 87), 26–27 (citing Ex. 1006, 53–54, 87–88);
- Statements that “Factor C of the present invention may have ***low susceptibility to inhibition of activity by an ion***” and “identif[ying] the claimed residual activity values of 10% or higher in the presence of 21 mM sodium citrate and 15% or higher in the presence of 16 mM magnesium sulfate as ‘***specific examples*** of ‘low susceptibility to inhibition of activity by an ion,’” PO Resp. 26 (citing Ex. 1006, 50–52); and
- Example that “details measuring the residual activity of Factor C recombinantly expressed in HEK293 cells in the claimed salt solutions of 21 mM sodium citrate and 16 mM magnesium sulfate,” including “procedure used for [the] measurement” and

results “demonstrating that expression of Factor C in HEK293 cells resulted in the claimed residual activity,” PO Resp. 14 (citing Ex. 1006, 96–99, 119, 122), 26–27 (citing Ex. 1006, 96–99, Fig. 4, Fig. 7).

We acknowledge that the ’767 application states, in its Modes for Carrying Out the Invention section, that “[t]he Factor C of the present invention is a Factor C derived from a horseshoe crab,” and states later in the same section that “[e]xamples of the horseshoe crab include . . . *Limulus polyphemus*.” Ex. 1006, 40. However, none of the remaining portions of ’767 application cited by Patent Owner relate directly to *L. polyphemus*; instead, the remaining portions of ’767 application cited by Patent Owner are directed to other species, in particular the Japanese horseshoe crab *T. tridentatus*. Further, Patent Owner’s witness, Dr. Schaefer, conceded that the ’767 application does not contain Factor C sequence information for *L. polyphemus*. See, e.g., Ex. 1067, 44:25–45:23.

Although “[n]o length requirement exists for a disclosure to adequately describe an invention,” *Falko-Gunter*, 448 F.3d at 1365–1366, we are persuaded that a POSA would not, based on the totality of the above disclosures, reasonably understand that the inventors were in possession of the claimed HEK-293 recombinant *L. polyphemus* Factor C protein, in view of the state of the art as of December 10, 2013. In this regard, we note that adequate written description of a biological molecule, such as a HEK293 recombinant *L. polyphemus* Factor C protein, requires “more than a mere statement that it is part of the invention and reference to a potential method for isolating it”; instead, what is required is “‘a precise definition, such as by structure, formula, chemical name, or physical properties,’ not a mere wish or plan for obtaining the claimed chemical invention.” *The Regents of the*

Univ. of California v. Eli Lilly & Co., 119 F.3d 1559, 1566–1567 (Fed. Cir. 1997) (quoting *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993)).

ii. State of the Art as of December 10, 2013

Citing *Falko-Gunter* as support, Patent Owner argues the fact that “the ’767 Application did not expressly recite [the *L. polyphemus* Factor C] sequence information is irrelevant to the written description analysis.” PO Resp. 16–17.

We acknowledge that “there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.” *Falko-Gunter*, 448 F.3d at 1366. However, *Falko-Gunter*, involving a claim to a vaccine comprising a poxvirus with an inactivating mutation in an “essential” gene, is factually distinguishable from the situation at hand.

First, the disclosure at issue in *Falko-Gunter* explicitly stated that “the invention can be applied to *any virus* where one or more essential gene(s) can be identified and deleted from or inactivated within the virus genome” and “provide[d] that ‘the virus may comprise . . . vaccinia virus,’ a type of poxvirus. *Falko-Gunter*, 448 F.3d at 1364. Second, and more importantly, the relevant DNA sequences in *Falko-Gunter* (i.e., the “essential” genes for poxvirus) were all well-known based on publicly available references. *Id.* at 1366. Thus, the Federal Circuit held in that case that, “where . . . **accessible** literature sources **clearly** provided, as of the relevant date, genes and their nucleotide sequences . . . , satisfaction of the written description requirement does not require either the recitation or incorporation by reference . . . of such genes and sequences.” *Id.* at 1368 (emphasis added).

In contrast, it is not disputed in this case that “there had not been, as of 2013, the full length cDNA sequence for *Limulus polyphemus* Factor C published.” *See, e.g.*, Tr. 48:18–19. Indeed, the ’498 PCT, which was filed by Patent Owner several years after December 10, 2013⁸ and shares two inventors with the ’318 patent, is titled “Recombinant Proteins Derived from the Limulus Bacterium, and DNA Molecules Encoding Same.” Ex. 1005, code (54). The ’498 PCT teaches that, even though the art has been motivated to produce recombinant horseshoe Factor C proteins in order to protect horseshoe crabs, and even though products utilizing such recombinant proteins have been commercialized, “all of these methods use recombinant proteins derived from organisms of the genus *Tachyplesus*” and “[t]here have been no reports of a reagent using recombinant proteins derived from *Limulus polyphemus*,” despite the fact that the latter is “widely used as a lysate reagent.” Ex. 1005 ¶¶ 8–9.

The ’498 PCT explains the reason for this is that “in *Limulus polyphemus*, the proteins and their genes involved in the mechanism of coagulation caused by endotoxin have not been completely identified structurally or functionally,” even though “more than 20 years have passed” since the report in 1991 of the complete gene and amino acid sequence of the *T. tridentatus* species of horseshoe crab. Ex. 1005 ¶¶ 10, 12; *see also id.* ¶ 13; Ex. 1069, 34:19–22 (Dr. Morris testifying that “creation of the recombinant protein requires the underlying sequence of . . . the original animal”). The ’498 PCT further explains that, “due to various differences and diversity of biomolecules depending on the genus and species of

⁸ The ’498 PCT was filed on October 18, 2017, and claims priority to JP2016-204729A, filed October 18, 2016. Ex. 1005, codes (22), (30).

horseshoe crab, it has not been possible to accurately determine the full-length sequence structure, expression, and function of these proteins and genes using conventional methods.” *Id.* ¶ 12.

Finally, the ’498 PCT states that its inventors “have succeeded in obtaining full-length cDNAs encoding all of the protein factors involved in the coagulation mechanism of *Limulus polyphemus*, ***something that no one had succeeded in doing for many years***, and in expressing all of the recombinant proteins, and have further discovered that these can be used for a variety of purposes, ***thereby completing the present invention.***” Ex. 1005 ¶ 17 (emphasis added). The ’498 PCT describes, as an aspect of its invention, a recombinant protein comprising a certain amino acid sequences recited therein and having Factor C activity, or a recombinant protein encoded by DNA comprising a base sequence having a specified degree of similarity with a recited DNA sequence. *Id.* ¶ 18. The disclosure in the ’498 PCT, several years after December 10, 2013, is thus compelling evidence that a POSA would not have reasonably understood the inventors to be in possession of a recombinantly produced *L. polyphemus* Factor C protein, as recited in claim 21, as of December 10, 2013.

Patent Owner argues that the statements in the ’498 PCT do not support a determination that the ’767 application fails to describe the claimed invention of the ’318 patent. Patent Owner argues that, “[a]lthough the inventors of the ’498 PCT may have been the first to identify the ***full-length*** cDNA sequence for *Limulus polyphemus* Factor C, other skilled artisans had the knowledge and means to do so as well.” PO Resp. 28 (citing Ex. 2036, 4; Ex. 1022, 152; Ex. 2035 ¶ 134; Ex. 2038 ¶¶ 61–81, 90–98).

This conclusion is belied by the disclosure in the '498 PCT itself. The '498 PCT explicitly states that, “due to the various differences and diversity of biomolecules depending on the genus and species of horseshoe crab, it ***has not been possible*** to accurately determine the full-length sequence structure, expression, and function of these proteins and genes ***using conventional methods.***” Ex. 1005 ¶ 12 (emphasis added). More importantly, the standard for adequate written description is whether a POSA would reasonably understand the inventors to have possessed the claimed invention as of the relevant date, in this case December 10, 2013. Even if a POSA ***could*** have determined the full-length cDNA sequence of *L. polyphemus* Factor C in December 2013, such a capability would not persuade us, in view of the totality of the record, that the POSA would have, based on the Specification, reasonably understood the inventors to ***be in possession*** of such a cDNA sequence or the recombinant protein encoded thereby.

In the Sur-reply, Patent Owner further argues that “Petitioner cites paragraphs from the '498 PCT that are not specific to Factor C, but instead more generally discuss ‘proteins and genes.’” Sur-reply 10–11. Although Patent Owner is correct that the '498 PCT does not limit its discussion of the difficulties in identifying the structure and function of *Limulus polyphemus* proteins and genes to Factor C, we see no reason why a POSA, reading the '498 PCT, would have understood the statements therein to exclude Factor C proteins and genes, given that it is not disputed that Factor C is one of the proteins involved in the mechanism of endotoxin coagulation in horseshoe crabs.

Patent Owner further argues that the written description of the '767 application is adequate in view of information well known in the art. PO

Resp. 15. Patent Owner argues that, by December 10, 2013, “researchers had not only successfully characterized Factor C protein from *Limulus polyphemus* amoebocytes . . . but also had compared it to Factor C from the *Tachypleus tridentatus* horseshoe crab,” and, furthermore, “a POSA would have understood that the coagulation cascade proteins (e.g., Factor C) were structurally similar and functionally identical across species.” PO Resp. 22–23 (citing Ex. 2038 ¶¶ 86–88, 91, 98–102; Exs. 2104–2106); *see also id.* at 15–16, 23–24 (citing evidence that the immunological and biochemical properties and amino acid compositions of *L. polyphemus* and *T. tridentatus* Factor C are indistinguishable and that the sequences of *Limulus* Factor C and those of Asian species are closely matched with >90% sequence identity) (quoting Ex. 1022, 150–151, 155; Ex. 2035, Abstract, ¶¶ 30, 32, 134; Ex. 2036, 4; Ex. 2049, 2), 27 (citing Ex. 2049, 2; Ex. 2038 ¶ 91).

Patent Owner argues that, by at least October 31, 2013, a large amount of *L. polyphemus* genomic data, including a 188 Mb cDNA amoebocyte transcriptome and a 4 Gb “shotgun sequence” of the genome would have been publicly available, and cites to the testimony of Dr. Schaefer that “a POSA as of December 10, 2013 would have been able to assemble **97.2% of the full Factor C coding sequence** based on known similarities between *Tachypleus tridentatus* and *Limulus polyphemus* [and] publicly available . . . sequence information.” PO Resp. 16 (citing Exs. 2050–54, 2057; Ex. 2038 ¶¶ 36, 37, 61–64). Dr. Schaefer further testified that a POSA “could have easily recovered the remaining sequence by applying standard methods well within the skill of a POSA.” *Id.* (citing Ex. 2038 ¶¶ 65–81); *see also id.* at 22.

None of the *L. polyphemus* sequence information Patent Owner points to, however, is within the four corners of the Specification. Nor do we find the sequence information of *L. polyphemus* Factor C protein to be “well known” in the art as were the essential genes for poxvirus at issue in *Falko-Gunter*. As an initial matter, Patent Owner’s arguments are contradicted by their own statements in the ’498 PCT. Moreover, even based on Patent Owner’s own arguments above, a skilled artisan would at best be able to “assemble” 97.2% of the full *L. polyphemus* Factor C coding sequence from disparate sources and would then have to “recover” the remaining sequence. Although adequate written description does not require actual reduction to practice, it nevertheless requires the inventors to *possess* the invention. *Falko-Gunter*, 448 F.3d at 1366–65.

The recent Federal Circuit decision in *Teva*, 172 F.4th 1367, which is in the context of an appeal from a judgment as a matter of law (JMOL), also does not support Patent Owner’s position.

In that case, the representative claim recited “[a] method for reducing incidence of or treating headache in a human, comprising administering to the human an effective amount of an anti-CGRP antagonist antibody, wherein said anti-CGRP antagonist antibody is a ... humanized monoclonal antibody.” *Teva*, 172 F.4th at 1372. The district court concluded, as a matter of law, that these claims were invalid for lack of written description and enablement, despite acknowledging that the jury could have permissibly found that murine anti-CGRP antagonist antibodies were disclosed in the specification and known in the art as of the relevant date, and that, furthermore, a POSA “would have (1) known methods for making murine anti-CGRP antagonist antibodies; (2) known that humanizing antibodies was routine; and (3) understood from the specification that *all* humanized anti-

CGRP antagonist antibodies would treat headache.” *Id.* at 1372–1373. The Federal Circuit reversed the JMOL.

Patent Owner argues that the *Teva* Court found written description support for humanized antibodies, which are not known in the art, by pointing to known murine antibodies and evidence that it was “routine” to humanize them. Paper 45, 2. Patent Owner argues that “[t]his discussion is relevant to one of PO’s arguments in support of written description that relies on publicly available deposit information and the ***routine*** procedures a POSA could employ to generate the full Factor C coding sequence for *L. polyphemus* Factor C and then recover the remaining sequence.”⁹ *Id.*

We disagree. The *Teva* Court confirmed that “‘a description that merely renders the invention obvious does not satisfy’ the written-description requirement,” but found that the specification at issue in *Teva* “did not merely render humanizing these antibodies obvious; it explicitly disclosed as much, along with how to do it, via prior-art methods that a reasonable jury could have found were routine.” *Teva*, 172 F.4th at 1377. Such is not the case here as evidenced by the disclosure of the ’498 PCT stating that the full-length cDNAs encoding all of the protein factors involved in the coagulation mechanism of *Limulus polyphemus* had not previously been achieved, and certainly not by December 10, 2013. *See* Ex. 1005 ¶ 17. Even more importantly, in reversing the JMOL, the *Teva* Court emphasized the claims on appeal “pertain[] to a well-known genus that is not, itself, the invention.” *Id.* at 1374. In contrast, here the

⁹ Patent Owner also argues that *Teva* is applicable to issues in this proceeding, specifically that “actual reduction to practice and examples are ***not*** required.” Paper 45, 1. As noted above, we do not disagree with this statement of the law.

recombinant HEK-293 *L. polyphemus* Factor C protein *is*, itself, the claimed invention.

iii. Petitioner's Statements in the '670 Opposition

Patent Owner asserts that arguments made by Petitioner in an Opposition filed against Patent Owner's European Patent No. 3530670 (EP '670) ("the '670 Opposition") "directly contravene" arguments made in the Petition, including with respect to the '498 PCT.¹⁰ PO Resp. 29–30; *see also* Sur-reply 4. Patent Owner notes Petitioner stated in the '670 Opposition that European Patent No. 2930241 (EP '241), which has the same specification as the '767 Application, "***already discloses 'a recombinant Factor C protein derived from Limulus polyphemus.***" PO Resp. 30 (citing Ex. 1048 ¶¶ 4, 51, 155).

Patent Owner further emphasizes that, in the Opposition, Petitioner characterized the statement in EP '670 that the *L. polyphemus* Factor C sequence could not be previously determined as "factually incorrect," and similarly characterized the assertion in that patent that the sequence could not be determined by general techniques as "entirely unsupported." PO Resp. 31 (citing Ex. 1048 9, n.2, ¶¶ 35, 75). Patent Owner asserts that, instead, Petitioner argued in the '670 Opposition that it would have been a matter of "routine analysis" to characterize the sequence of *Limulus polyphemus* Factor C. Sur-reply 4 (citing Ex. 1048 ¶¶ 30–37, 56, 59), 12 (citing Ex. 1048, 9, n.2, ¶¶ 35, 75).

¹⁰ EP '670 is based on PCT application PCT/JP2017/037629, which was published as the '498 PCT. Ex. 1048 ¶ 6.

We have considered Petitioner's statements in the '670 Opposition,¹¹ including those cited above, and have given some weight to Patent Owner's arguments that they support a determination the '767 application adequately describes the claimed recombinant *L. polyphemus* Factor C protein. However, adequate written description has specific requirements under United States patent law. Because Petitioner's statements in the '670 Opposition are made in a different legal context, they do not outweigh the other evidence of the record showing that the '767 application does not reasonably convey inventor's possession of the *L. polyphemus* Factor C sequence, including Patent Owner's statements in the '498 PCT that also appear to be contradictory to the position Patent Owner has taken in this proceeding.¹²

¹¹ In support of the '670 Opposition, Petitioner also filed a Declaration of Michael A. Frohman, MD, PhD (Ex. 2004, "Frohman Declaration"). Ex. 1048, 3.

¹² Patent Owner cites *Provepharm Inc. v. Wista Lab 'ys. Ltd.*, IPR2018-00323, 2019 WL 2865314, *15 (PTAB July 2, 2019) to argue that "Petitioner's contradictory statements before the EPO at the very least 'significantly weaken and undermine the credibility of Petitioner's case.'" PO Resp. 5. *Provepharm* is neither controlling nor analogous to the facts of this case. In *Provepharm*, Petitioner asserted in appealing the EPO's rejection of its EP application, that "normal physico-chemical separation techniques could *not* purify a methylene blue produced by conventional processes," while arguing in the *inter partes* proceeding that "an ordinarily skilled artisan would have had a reasonable expectation of success in using routine HPLC to purify methylene blue to obtain at least 98% purity" to render the patent at issue in that proceeding obvious. *Provepharm*, 2019 WL 2865314, at *13–*15. Here, putting aside the issue that Petitioner's statements in the '670 Opposition and in this proceeding are directed to different time frames, it is not necessarily contradictory that (1) a POSA is able to obtain the sequence of *L. polyphemus* Factor C protein using known techniques and (2) the '318 patent did not reasonably convey to a skilled

For instance, although the Notice of Opposition in the '670 Opposition states that EP '241 “discloses” a recombinant Factor C protein derived from *Limulus polyphemus*, there is no evidence that “disclose” in the context in which the statement is made carries the same meaning as adequate disclosure under 35 U.S.C. § 112. Furthermore, as discussed above, even if Petitioner’s statements in the '670 Opposition suggest that a POSA *could* have determined the *L. polyphemus* Factor C sequence with general techniques or that to do so would have been obvious, this does not suggest that the *L. polyphemus* Factor C sequence is “well known” within the meaning of *Falko-Gunter*, or outweigh the evidence of record that the disclosure *in the '767 application* does not reasonably convey to a POSA that the inventors were in possession of the sequence as of December 10, 2013.

We are persuaded, based on the entirety of the evidence of record, that a POSA would not have reasonably understood the inventors of the '318 patent to be in possession of the complete invention in December 2013. *See Ariad Pharms.*, 598 F.3d at 1340.

artisan that the inventors were in possession of the sequence. *Ariad*, 598 F.3d at 1352 (explaining that, “while the description requirement does not demand any particular form of disclosure, or that the specification recite the claimed invention *in haec verba*, a description that merely renders the invention obvious does not satisfy the requirement”) (citation omitted); *id.* at 1352 (explaining that, “although written description and enablement often rise and fall together, requiring a written description of the invention plays a vital role in curtailing claims that do not require undue experimentation to make and use, and thus satisfy enablement, but that have not been invented, and thus cannot be described”).

iv. Disclosure of Claimed Functional Limitations

The parties also dispute whether, regardless of whether a POSA would have had reasonably understood the inventors to be in possession of a HEK293 *L. polyphemus* Factor C protein, they would have reasonably understood the inventors to be in possession of such a protein ***with the claimed functional requirements***, i.e., one exhibiting residual activity of (1) 10% or higher in the presence of 21 mM sodium citrate; and/or (2) 15% or higher in the presence of 16 mM magnesium sulfate. *See, e.g.*, Pet. 23–31; PO Resp. 17–27.

Because we find that a POSA would not have reasonably understood the inventors to be in possession of a recombinant HEK293 *L. polyphemus* Factor C protein, we similarly find that a POSA would not have reasonably understood the inventors to be in possession of such a protein with the recited functional limitations of residual activity values.¹³

¹³ It is not clear whether Patent Owner is taking the position that the residual activity of a recombinant *L. polyphemus* protein is an inherent property. In its Response, Patent Owner cites *Allergan* for the proposition that “[a] claim that recites a property that is necessarily inherent in a formulation that is adequately described is not invalid as lacking written description merely because the property itself is not explicitly described.” PO Resp. 21 (citing *Allergan, Inc. v. Sandoz, Inc.*, 796 F.3d 1293 (Fed. Cir. 2015)). However, during oral argument Patent Owner’s counsel clarified that this is not a position Patent Owner has taken in its papers. Tr. 62:2–19. Regardless of whether residual activity is an inherent property of the HEK293 recombinant *L. polyphemus* Factor C protein, we find that the ’767 application does not adequately disclose the HEK293 recombinant *L. polyphemus* Factor C protein itself.

2. Enablement

Petitioner and Patent Owner also dispute whether the '767 application provides enabling disclosure for claim 21. *See, e.g.*, Pet. 35–42; PO Resp. 31–44.

To establish priority to December 10, 2013, the '767 application must satisfy ***both*** the written description and enablement requirements of Section 112(a). Because we find that the '767 application does not adequately describe the claimed HEK293 recombinant *L. polyphemus* Factor C protein, we need not, and do not, address the issue of whether the '767 application also does not enable a POSA to make and use the full scope of the claimed Factor C protein without undue experimentation.

Having determined that the '767 application does not provide adequate written description of the invention of challenged claim 21, we find Petitioner has established by a preponderance of evidence that Mizumura, the '498 PCT, and McClymont were publicly available before the effective filing date of the challenged claim. We proceed to analyze Petitioner's obviousness grounds on that basis.

F. Ground 1: Obviousness over Mizumura and the '498 PCT

The parties agree that Mizumura's disclosure is identical to that of the '767 application and the '318 patent specification. Pet. 45; PO Resp. 45. Petitioner asserts, and Patent Owner has not disputed, that the '498 PCT is an international publication disclosing the production of *Limulus polyphemus* recombinant Factor C via a mammalian recombinant expression system. Pet. 45.

1. Petitioner's Position

Petitioner maps each element of claim 21 to disclosures in Mizumura and/or the '498 PCT in the Petition. Pet. 48–52.

Petitioner argues that, by the April 26, 2018 publication date of the '498 PCT,

a POSA considering Mizumura's data on HEK293 produced recombinant Factor C from *Tachypleus tridentatus*, as well as the '498 PCT's explicit disclosure of production of functional *Limulus polyphemus* recombinant Factor C in HEK293 cells would have reason—including the wide adoption of and reliance upon the LAL test but also including the specificity challenges with that test and the desire to avoid contaminants associated with the natural lysate—to develop a recombinant Factor C protein with a residual activity value similar to that shown in Mizumura's FIG. 7 **for *Limulus polyphemus*** species of horseshoe crab.

Pet. 56 (citing, e.g., Ex. 1002 ¶¶ 176–177).

Petitioner cites to Dr. Jain's testimony and McClymont to argue that having the full-length cDNA and amino acid sequence of the *L. polyphemus* Factor C protein “would have allowed a POSA to compare them with gene and amino acid sequences of other, well-studied species such as *Tachypleus tridentatus*, to make reasonable predictions about whether recombinantly-produced proteins would exhibit similar functional characteristics such as ‘residual activity.’” Pet. 57 (citing, e.g., Ex. 1002 ¶¶ 179–180; Ex. 1010, 38, 48). Petitioner further cites the 2018 testimony of Dr. Mizumura, an inventor of the '318 patent, to support its arguments that a POSA would have had reasonable expectation of success regarding recombinantly produced *L. polyphemus* Factor C protein having the residual activity recited in claim 21. *Id.* at 59–60 (citing Ex. 1002, ¶¶ 188–189; Ex. 1029, 2–4).

2. Patent Owner's Position

Patent Owner first argues that Mizumura and the '498 PCT are not prior art because claim 21 was effectively filed December 10, 2013. PO Resp. 44. We disagree for the reasons already discussed above. *See supra* Section II.E.

Patent Owner asserts that, even if Mizumura and the '498 PCT are prior art, Petitioner's invalidity challenge fails because Petitioner fails to show that the prior art teaches or suggests the claimed residual activity limitations. Patent Owner argues that "Petitioner has failed to demonstrate anything in the prior art disclosing the claimed residual activity for the specifically claimed *limulus polyphemus* factor C expressed in HEK293 cells." PO resp. 45; *see also* Sur-reply 14–16.

Patent Owner acknowledges Petitioner's assertion that a POSA would have had reason to modify Mizumura with the teachings of the '498 PCT, with a reasonable expectation of success of achieving a HEK-293 recombinant *L. polyphemus* horseshoe crab Factor C protein with the claimed residual activity. However, Patent Owner argues that this assertion "directly contradicts" Petitioner's arguments, in the context of determining the effective filing date of claim 21, that "residual activity data in *Tachypleus tridentatus* Factor C is insufficient to show that the claimed residual activity would be maintained for *Limulus polyphemus* factor C." PO Resp. 46; *see also* Sur-reply 14. Patent Owner points to Petitioner's assertion, in arguing against the December 10, 2013, priority date of the '318 patent, that "non-conservative mutations between the species would have had the 'potential to cause structure and function differences between the recombinantly produced Factor C proteins.'" PO Resp. 47. Patent Owner argues that this, together with "Petitioner's failure to present any analysis of

the percentage of non-conservative mutations between species,” defeats Petitioner’s attempt to demonstrate a reasonable expectation of success. *Id.* at 47–48.

Patent owner argues that Petitioner’s reasonable expectation of success argument is “nothing more than conclusory assertions with no support.” PO Resp. 46. Patent Owner asserts that “Petitioner’s reliance on a statement made by Dr. Mizumura in a declaration submitted during prosecution of the ’767 Application fails to fill the gap in the analysis.” *Id.*

3. Analysis

For the reasons below, we are persuaded that Petitioner has met its burden to show that a POSA would have had a reasonable expectation of success in combining Mizumura and the ’498 PCT to arrive at a HEK293 recombinant *L. polyphemus* Factor C protein.

As noted above, Petitioner’s arguments for the limitations relating to residual activity are based on what a POSA would have reasonably expected when combining Mizumura, with its disclosure of the residual activities of recombinant horseshoe crab Factor C proteins, particularly the HEK293 recombinant Factor C protein of *T. tridentatus*, with the disclosure in the ’498 PCT, particularly the full-length sequence for the claimed *L. polyphemus* Factor C protein disclosed in the ’498 PCT. Pet. 57.

In addition to Dr. Jain’s testimony, Petitioner cites to, for instance, McClymont, which explained that “[d]etermining the sequence for [*L. polyphemus* Factor C] also allowed comparisons to be made between the different species to identify any differences that may exist” and to make reasonable predictions about their function. Pet. 57–58 (citing Ex. 1010, 48, which relies on the high-level of similarity between the N-terminal regions

of three different horseshoe crab species to support the assumption that all three proteins will function in a similar manner, albeit with respect to the binding of lipid A rather than with respect to residual activity).

Likewise, Petitioner cites to Dr. Mizumura's testimony in a February 22, 2018, Declaration, which provided an alignment of the Factor C of *T. tridentatus* (TtFC) and the Factor of *L. polyphemus* (LpFC) sequences, with "consensus sequences which an undergo N-type sugar chain (N-lined sugar chain) modification . . . underlined." Ex. 1029, 4 (cited at Pet. 60). In that declaration, Dr. Mizumura states:

The similarity between the amino acid sequence of TtFC and that of LpFC is 99.5%. Further, the amino acid residues which can undergo N-type sugar chain modification are conserved. Some amino acid residues of the N-type sugar chain modification site of TtFC are substituted in that of LpFC, however, the function as the N-type sugar chain modification site is conserved.

. . . .

. . . [T]he above-described evidence supports that the Factor C of *Limulus polyphemus* would also have unexpectedly superior property of being less susceptible to inhibition by ions, as exhibited by Factor C of *Tachypleus tridentatus*.

Ex. 1029, 4–5.

We disagree with Patent Owner's assertion that Petitioner's arguments against the December 10, 2013, priority date, that "non-conservative mutations between the species would have had the 'potential to cause structure and function differences between the recombinantly produced Factor C proteins,'" together with "Petitioner's failure to present any analysis of the percentage of non-conservative mutations between species," defeats Petitioner's attempt to demonstrate a reasonable expectation of success. PO Resp. 47–48.

“[E]xpectation of success need only be reasonable, not absolute.” *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007). Neither do we see Petitioner’s arguments regarding the December 10, 2013 priority date to be “mutually opposed” as Dr. Schaefer testified. Ex. 1067, 216:4–24. Instead, we credit evidence of record, including Dr. Jain’s testimony and the February 22, 2018 Mizumura Declaration, that existence of the full sequence would permit a more complete analysis and that such an analysis would provide a POSA with a reasonable expectation that the claimed *L. polyphemus* recombinant protein would have a residual activity within the claimed range. *See, e.g.*, Ex. 1029, 2–5; Ex. 1010, 48; Ex. 1065, 117:14–130:24 (explaining that comparison of partial sequences in the Tokunaga 1991 publication showed “difference around the cleavage site” between *T. tridentatus* and *L. polyphemus* but comparison of the full sequence revealed that “the catalytic triad of histidine, serine, aspartate . . . to be more similar between *Tachypleus* and *Limulus*”).

Patent Owner asserts that “Petitioner’s reliance on a statement made by Dr. Mizumura in a declaration submitted during prosecution of the ’767 Application fails to fill the gap in the analysis” regarding reasonable expectation of success, because the declaration “offers no evidence of the percentage of conserved amino acid substitutions that exist to support the conclusion that a POSA would have expected residual activity to be maintained between *Tachypleus tridentatus* and *Limulus polyphemus*” PO Resp. 47.

However, as noted above, Dr. Mizumura provides an alignment of Factor C proteins from the two different species of horseshoe crab, determines that the similarity between the amino acid sequence is 99.5%, states that the amino acid residues that can undergo N-type sugar chain

modifications are conserved, *and* concludes that the above evidence supports that *L. polyphemus*, like *T. tridentatus*, would also be less susceptible to inhibition by ions. Ex. 1029, 4–5.

For the reasons discussed above, we also disagree with Patent Owner’s assertion that Petitioner’s reasonable expectation of success argument is “nothing more than conclusory assertions with no support.” PO Resp. 46. Rather, we find Petitioner has shown, by a preponderance of the evidence, that a POSA would have had reason to combine the teachings of Mizumura and the ’498 PCT, with a reasonable expectation of success in arriving at the Factor C protein recited in claim 21.

G. Ground 2: Obviousness over Mizumura and McClymont

Petitioner asserts that, “[a]s with the ’498 PCT, McClymont discloses the full cDNA and amino acid sequence for *Limulus polyphemus* Factor C protein and discloses expressing such protein using several common expression systems (including yeast and insect cells).” Pet. 60 (citing Ex. 1010, 84–96, 159–60 (Appx. B)). Petitioner and Patent Owner make substantially identical arguments for this Ground as for Ground 1, except that McClymont is cited in place of the ’498 PCT as disclosing “the full gene coding and amino acid sequences of *L. polyphemus* Factor C protein.” Pet. 60–61; PO Resp. 48–49; Reply 24; Sur-reply 16.

For the same reasons discussed in Ground 1, we are persuaded that Petitioner has shown, by a preponderance of the evidence, that a POSA, combining the teachings of Mizumura and McClymont, would have had reason to combine the cited references with a reasonable expectation of success in arriving at the Factor C protein recited in claim 21.

H. Objective Indicia of Non-Obviousness

Patent Owner argues that objective indicia, or so-called secondary considerations, of non-obviousness, in particular unexpected results, also supports a finding that claim 21 is not obvious. PO Resp. 49. More particularly, Patent Owner asserts that “Factor C from *Limulus polyphemus* exhibits unexpectedly superior residual activity values in the claimed 21 mM sodium citrate and 16 mM magnesium sulfate solutions as compared to the residual activity observed for Factor C from *Tachypleus tridentatus*.” *Id.* at 50.

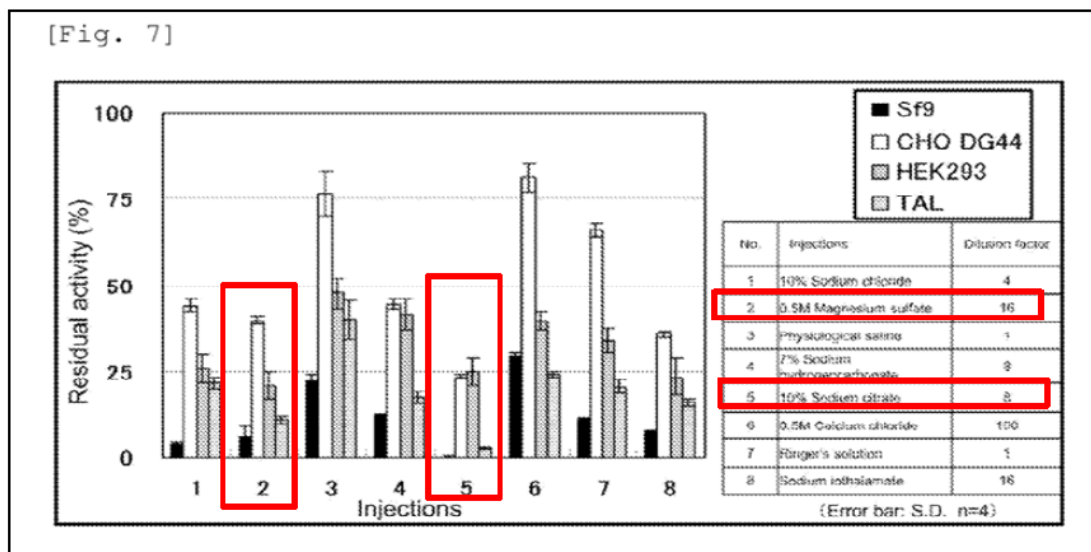
Secondary considerations of non-obviousness, including unexpected results, must be taken into account when present. *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014). “However, ‘[f]or objective evidence of secondary considerations to be relevant, there must be a nexus between the merits of the claimed invention and the objective evidence.’” *Bayer Pharma Aktiengesellschaft v. Mylan Pharms. Inc.*, 152 F.4th 1400, 1407 (Fed. Cir. 2025) (quoting *Volvo Penta of the Ams., LLC v. Brunswick Corp.*, 81 F.4th 1202, 1210 (Fed. Cir. 2023)). “Where the offered secondary consideration actually results from something other than what is both claimed and *novel* in the claim, there is no nexus to the merits of the claimed invention.” *Id.* (quoting *In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011)). A patentee bears the burden of production to show unexpected results. *Zup, LLC v. Nash Mfg., Inc.*, 896 f.3d 1365, 1373 (Fed. Cir. 2018).

We analyze Patent Owner’s proffered evidence of unexpected results with these standards in mind.

1. Residual Activities in Factor C Recombinantly Produced in CHO DG44

Patent Owner first compares the residual activity of *Limulus polyphemus* Factor C recombinantly produced in CHO DG44 cells, as set forth in Figure 1 of the Mizumura Declaration submitted during prosecution of the '318 patent, with the residual activity of *Tachypleus tridentatus* Factor C recombinantly produced in CHO DG44 cells, as set forth in Figure 7 of Mizumura. PO Resp. 50–52 (comparing Ex. 1004, 85 (Fig. 1) with Ex. 1009, 122 (Fig. 7)).

Mizumura Figure 7 and Figure 1 from the Mizumura Declaration are reproduced below with Patent Owner's annotations:



PO Resp. 51 (reproducing Ex. 1009, Fig. 7 with annotations).

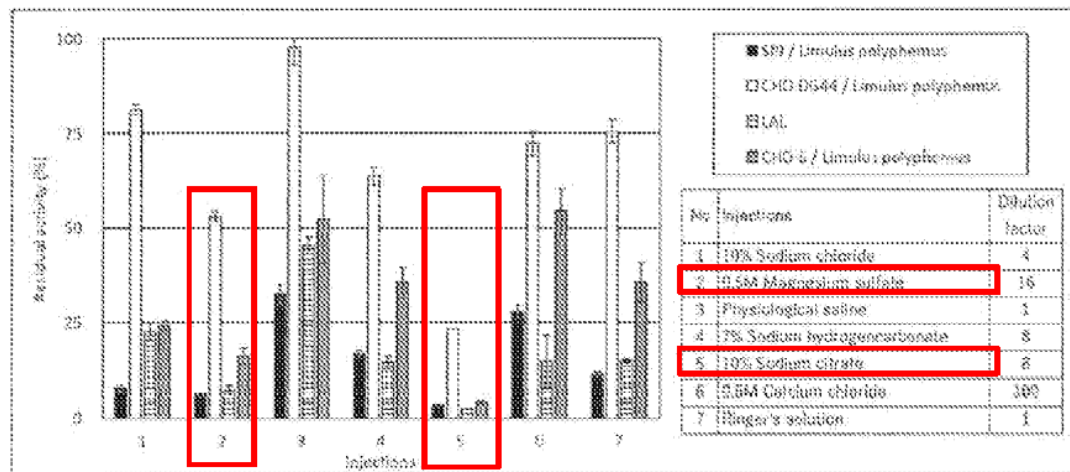


Fig. 1. Residual Activity of *L. polyphemus* Factor Cs in the Presence of Salt

PO Resp. 52 (reproducing Ex. 1004, Fig. 1 with annotations).

Patent Owner asserts that, based on the data in Figure 7, the residual activities of *T. tridentatus* Factor C protein recombinantly produced in CHO DG44 cells are approximately 40% and 25%, respectively, in 16 mM magnesium sulfate and 21 mM sodium citrate. PO Resp. 51; *see also* Ex. 2042 ¶ 44. Patent Owner asserts that, based on the data in Figure 1 of the Mizumura Declaration submitted during the '318 patent prosecution, the residual activity of *L. polyphemus* Factor C protein recombinantly produced in CHO DG44 cells is approximately 50–55% in the presence of 16 mM magnesium sulfate. PO Resp. 52; *see also* Ex. 2042 ¶ 47.

Patent Owner argues that, “[w]hen comparing the residual activity for recombinantly produced *Limulus polyphemus* Factor C in CHO DG44 cells with recombinantly produced *Tachypleus tridentatus* Factor C in CHO DG44 cells, the *Limulus polyphemus* Factor C exhibits unexpectedly superior residual activity to *Tachypleus tridentatus*.” PO Resp. 52 (citing Ex. 2042 ¶¶ 43–48, 51).

We are not persuaded. As noted above, evidence of unexpected results is only relevant if there is a nexus between the claimed invention and

the objective indicia. *In re Affinity Labs of Tex., LLC*, 856 F.3d 883, 901 (Fed. Cir. 2017). There is no nexus unless the evidence presented is reasonably commensurate with the scope of the claims. *Id.* In this case, the alleged unexpected results are not exhibited by the claimed Factor C protein, i.e., *Limulus polyphemus* Factor C recombinantly expressed in HEK293 cells, but rather *Limulus polyphemus* Factor C recombinantly expressed in CHO DG44, a different type of cell.

Neither has Patent Owner provided persuasive evidence as to the nexus between the alleged unexpected results and the claimed recombinant Factor C protein. Patent Owner's expert, Dr. Morris, testified that, because *T. tridentatus* and *L. polyphemus* have been consistently considered functionally equivalent in terms of activity, "[a] POSA would have expected this equivalence to carry forward into the recombinant expression system and not find one species being unexpectedly superior over the other." Ex. 2042 ¶¶ 49–50. In its Sur-reply, Patent Owner also asserted that data in the Mizumura Declaration is relevant because, "[w]hile the Mizumura Declaration provided data in CHO cells, the data is for the *claimed Limulus polyphemus* Factor C" and was cited "to demonstrate that, as compared to the closest prior art (Mizumura) that uses non-claimed *Tachypleus tridentatus* Factor C, the claimed *Limulus polyphemus* Factor C exhibits unexpectedly superior residual activity." Sur-reply 16–17.

However, claim 21 does not claim all recombinant *Limulus polyphemus* Factor C, only those recombinantly expressed in HEK293. Patent Owner's arguments and Dr. Morris's testimony do not explain why any allegedly unexpected results exhibited by *L. polyphemus* Factor C protein in one recombinant expression system would have a nexus (e.g.,

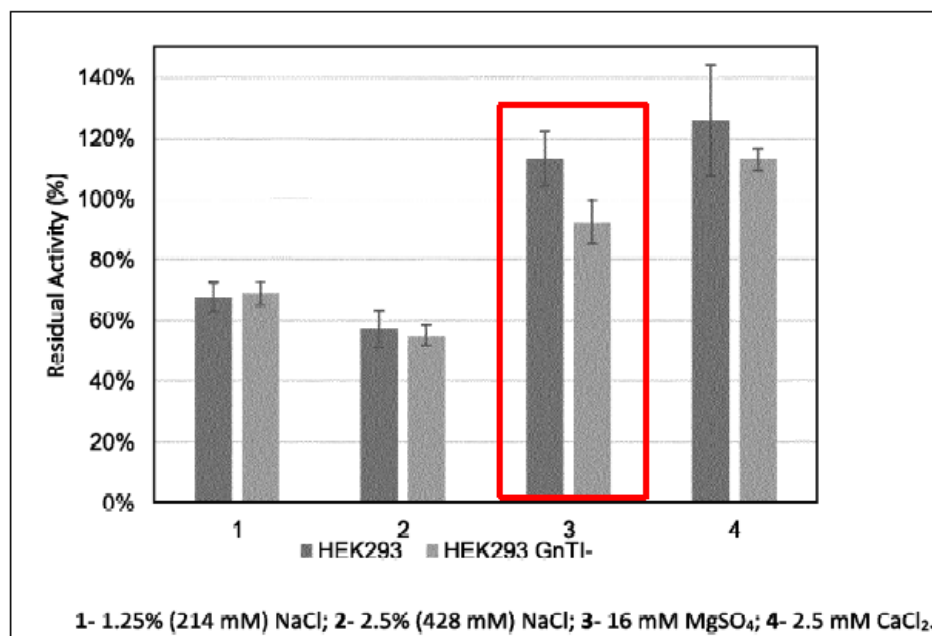
would be expected to carry over) to *L. polyphemus* Factor C protein expressed in a *different*, claimed expression system.

In view of the above, we accord little weight to the above evidence of allegedly unexpected results.

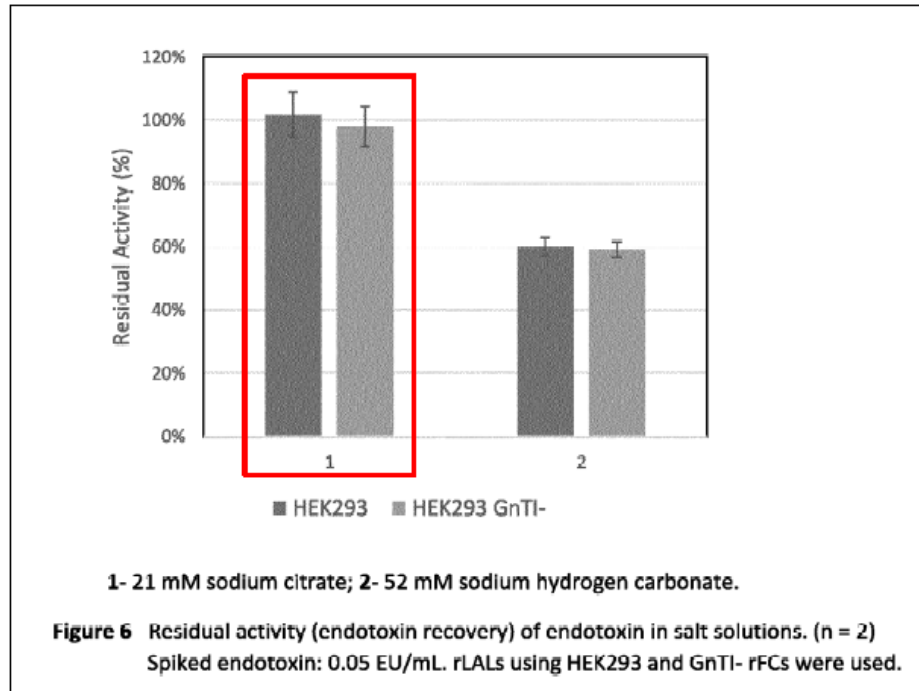
2. Comparison with Data from Exhibit 2033

Patent Owner also compares Mizumura Figure 7 with data submitted as part of a European Opposition proceeding filed against EP3441466 (EP '466) ('466 Opposition). PO Resp. 53–56 (comparing Ex. 2033 with Ex. 1009, Fig. 7).

Figures 4 and 6 of Exhibit 2033 is reproduced below with Patent Owner's annotations:



PO Resp. 54 (reproducing Ex. 2033, Fig. 4 with annotations).



PO Resp. 55 (reproducing Ex. 2033, Fig. 6 with annotations).

Patent Owner asserts that the above figures show “*Limulus polyphemus* recombinantly produced in HEK293 cells exhibited residual activity between 90-120% (inclusive of error bars) in 16 mM magnesium sulfate (Fig. 4) and . . . between 90-110% (inclusive of error bars) in 21 mM sodium citrate (Fig. 6).” PO Resp. 55; *see also* Ex. 2042 ¶¶ 53–54. Patent Owner asserts that these residual activities are far superior to the residual activities reported in Figure 7 of Mizumura for the closest prior art, i.e., *T. tridentatus* Factor C proteins recombinantly produced in HEK293 cells, which “demonstrated approximately 20-25% residual activity in 16 mM magnesium sulfate . . . and about 20-30% residual activity in 21 mM sodium citrate.” PO 55–56 (citing Ex. 2042 ¶ 54). Patent Owner asserts that a POSA would not have expected this magnitude of difference in residual activities between the two strains of Factor C, demonstrating that the claimed invention exhibits unexpected results. *Id.* at 56.

Because the horseshoe crab Factor C protein tested in Exhibit 2033 is encompassed by claim 21, i.e., a horseshoe crab Factor C protein wherein the horseshoe crab is *L. polyphemus* and wherein the protein is recombinantly expressed from a HEK293 cell, we give this evidence some weight. We likewise give it some weight because we find the residual activities disclosed for recombinant HEK293 *L. polyphemus* Factor C protein in Exhibit 2033 (~90–120% in 16 mM magnesium sulfate and ~90–110% in 21 mM sodium citrate) to be significantly higher than those disclosed in Mizumura Figure 7 for recombinant HEK293 *T. tridentatus* Factor C protein (~20–25% in 16 mM magnesium sulfate and ~20–30% in 21 mM sodium citrate).

However, as Petitioner points out, it is not clear that the experiments in Mizumura Figure 7 and Exhibit 2033 were performed in comparable conditions. Indeed, Dr. Morris agreed that, although some conditions may be assumed to be the same, “many of the conditions that were used to generate the results in [Exhibit 2033] were different from those . . . used in generating the data in [Mizumura] Fig. 7.” Ex. 1069, 160:6–171:9.

Petitioner further introduced evidence, with which Dr. Morris agreed, that comparing the results of endotoxin testing using recombinant Factor C and using traditional *Limulus* amebocyte lysate (LAL) “requires careful study design to reach accurate conclusions”; that such comparative studies are “inherently difficult to conduct, because the variation in results within any type of endotoxin testing is relatively high because of the very low (subpicogram) level tested and the tremendous sensitivity of the assay”; and that “[m]inor differences in procedure (temperature, mixing time and operators) result in significant variation, even when the same LAL method is

used on the same samples at the same time in the same laboratory.”

Ex. 2062, 605; Ex. 1069, 125:16–129:21.

Although the specific context of the statements above is with respect to comparisons of recombinant Factor C and LAL, Dr. Morris acknowledges that procedural differences may also impact comparisons between assays using two different recombinant Factor C proteins. *See, e.g.*, Ex. 1069, 155:11–157:16, 160:12–171:9.

In its Sur-reply, Patent Owner does not provide further rebuttal to the substance of the evidence discussed above, but argues that “[n]otably absent from Petitioner’s critique of this data is its admission that the data in [Exhibit 2033] appears to come from *Petitioner’s own experimental work*.” Sur-reply 17 (comparing Ex. 2033, 4 with Ex. 2034, Fig. 5, ¶ 42). Assuming the work in Exhibit 2033 was performed by Petitioner, this fact would not obviate the issue with respect to whether, in view of the differing conditions under which the assays were performed and evidence that such conditions may affect assay results, it is appropriate to compare the data in Exhibit 2033 and Mizumura Figure 7 for purposes of showing unexpected results.¹⁴

Accordingly, although we accord Patent Owner’s evidence of unexpected results some weight, we find that a preponderance of the evidence of record nevertheless supports a determination that claim 21 is obvious.

¹⁴ To the extent Patent Owner’s complaint is that Petitioner should have produced information relating to Exhibit 2033 as routine or additional discovery, we note that Patent Owner has not requested authorization to move to compel such discovery.

I. Summary

In sum, we find that claim 21 is not entitled to a priority date of December 10, 2013, and that Mizumura, the '498 PCT, and McClymont qualify as prior art. We also find Petitioner has shown, by a preponderance of the evidence, that the combination of the asserted prior art teaches or suggests each limitation of claim 21. Petitioner also has shown, by a preponderance of the evidence, that an ordinarily skilled artisan would have had a reason to combine those teachings with a reasonable expectation of success of arriving at the claimed invention before its effective filing date. In addition, having accorded Patent Owner's evidence of objective indicia its proper weight, we nevertheless find it does not, when considered together with the evidence of obviousness, show claim 21 to be non-obvious. As a result, we find Petitioner has shown, by a preponderance of the evidence, that the combination of the teachings of Mizumura with those of the '498 PCT or McClymont renders claim 21 obvious.

III. PATENT OWNER'S REVISED CONTINGENT MOTION TO AMEND

A. Principles of Law

Because we conclude that claim 21 is unpatentable, we consider Patent Owner's Revised Contingent Motion to Amend. *See* RMTA 1 (stating that, "[s]hould the Board hold claim 21 unpatentable, PO submits that this Motion demonstrates the patentability of substitute claim 22 presented herein").

"Before considering the patentability of any substitute claims, . . . the Board first must determine whether the motion to amend meets the statutory and regulatory requirements set forth in 35 U.S.C. § 316(d) and 37 C.F.R. § 42.121." *Lectrosonics, Inc. v. Zaxcom, Inc.*, IPR2018-01129, Paper 15 at 4

(PTAB Feb. 25, 2019) (precedential). Accordingly, a patent owner must provide a claim listing reproducing each proposed substitute claim, and must make an initial showing to demonstrate the following: (1) the amendment proposes a reasonable number of substitute claims; (2) the proposed claims are supported in the original disclosure (and any earlier filed disclosure for which the benefit of the earlier filing date is sought); (3) the amendment responds to a ground of unpatentability involved in the trial; and (4) the amendment does not seek to enlarge the scope of the claims of the patent or introduce new subject matter. *See* 35 U.S.C. § 326(d); 37 C.F.R. § 42.121.

If the *Lectrosonics* requirements are met, the Board also must assess the patentability of proposed substitute claims. *Aqua Prods., Inc. v. Matal*, 872 F.3d 1290, 1328 (Fed. Cir. 2017) (en banc). A patent owner does not bear the burden of persuasion to show that the proposed substitute claims are patentable. *Id.* at 1328; *Bosch Automotive Service Solutions, LLC v. Matal*, 878 F.3d 1027 (Fed. Cir. 2017), amended by *Bosch Automotive Service Solutions, LLC v. Iancu*, No. 2015-1928 (Fed. Cir. Mar. 15, 2018); *Lectrosonics*, Paper 15 at 3–4. Rather, ordinarily “the petitioner bears the burden of proving that the proposed amended claims are unpatentable by a preponderance of the evidence.” *Bosch*, 878 F.3d at 1040 (as amended on rehearing); *Lectrosonics*, Paper 15 at 3–4.

To determine whether a petitioner has proven the substitute claims are unpatentable, the Board focuses on “arguments and theories raised by the petitioner in its petition or opposition to the motion to amend.” *Nike, Inc. v. Adidas AG*, 955 F.3d 45, 51 (Fed. Cir. 2020). The Board itself also may justify any finding of unpatentability by referring to evidence of record in the proceeding. *Lectrosonics*, Paper 15 at 4 (citing *Aqua Products*, 872 F.3d at 1311 (O’Malley, J.)).

B. Proposed Substitute Claim 22

Patent Owner proposes substitute claim 22, reproduced below with underlining to indicate text added relative to original claim 21 and double bracket to indicate text removed relative to original claim 21:

Claim 22. [Proposed substitute for claim 21] A horseshoe crab Factor C protein having activity of Factor C,
wherein the horseshoe crab is *Limulus polyphemus*, and
wherein the horseshoe crab Factor C protein is produced through being recombinantly expressed from a Human Embryonic Kidney (HEK) 293 cell, and
wherein the Factor C protein exhibits a residual activity of at least one selected from the group consisting of:
(1) [[10% or higher in the presence of 21 mM sodium citrate]] a residual activity in the presence of 21 mM sodium citrate that is:
(i) higher than the residual activity in the presence of 21 mM sodium citrate of a corresponding Limulus polyphemus Factor C protein expressed in Sf9 as a host cell, or
(ii) higher than the residual activity in the presence of 21 mM sodium citrate of a native Limulus polyphemus Factor C protein,
wherein the horseshoe crab Factor C protein is not a horseshoe crab Factor C protein having less than 10% residual activity in the presence of 21 mM sodium citrate; and
(2) [[15% or higher in the presence of 16 mM magnesium sulfate]] a residual activity in the presence of 16 mM magnesium sulfate that is:
(i) higher than the residual activity in the presence of 16 mM magnesium sulfate of a corresponding Limulus polyphemus Factor C protein expressed in Sf9 as a host cell, or
(ii) higher than the residual activity in the presence of 16 mM magnesium sulfate of a native Limulus polyphemus Factor C protein,

wherein the horseshoe crab Factor C protein is not a horseshoe crab Factor C protein having less than 15% residual activity in the presence of 16 mM magnesium sulfate.

RMTA Appx A-1.

C. Requirements Under 35 U.S.C. § 316 and 37 C.F.R. § 42.121

1. Reasonable Number of Substitute Claims

A motion to amend must propose a reasonable number of substitute claims. 35 U.S.C. § 316(d)(1)(B); 37 C.F.R. § 42.121(a)(3).

Patent Owner proposes to substitute claim 22 for claim 21 if claim 21 is found to be unpatentable. RMTA 1, Appx A-1. The proposed one-to-one substitution is reasonable. *See* 37 C.F.R. § 42.121(a)(3) (“The presumption is that only one substitute claim would be needed to replace each challenged claim, and it may be rebutted by a demonstration of need”).

2. Respond to Ground of Unpatentability

A motion to amend must respond to a ground of unpatentability involved in the proceeding. 37 C.F.R. § 42.121(a)(2)(i).

Patent Owner asserts that proposed substitute claim 22 “responds to Petitioner’s arguments that claim 21 of the ’318 Patent is not entitled to its December 10, 2013 priority date.” *See* RMTA 1. Patent Owner contends the amendments narrows certain limitations “to overcome the priority date challenge, thus rendering Petitioner’s unpatentability Grounds 1 and 2 moot because the relied upon references are not prior art.” *Id.* at 2. Petitioner does not dispute Patent Owner’s proposed amendments attempt to respond to a ground of unpatentability. *See generally* RMTA Opp.

We find Patent Owner has met this requirement by amending claim 21 to address Petitioner’s arguments regarding priority date based on the residual activity limitations.

3. Scope of Amended Claim

A motion to amend may not enlarge the scope of the claims of a patent. 35 U.S.C. § 316(d)(3); 37 C.F.R. § 42.121(a)(2)(ii). Patent Owner notes original claim 21 requires the *Limulus polyphemus* Factor C protein expressed from HEK293 to exhibit a residual activity of “‘at least one selected from a group consisting of’ . . . (i) 10% or higher in the presence of 21 mM sodium citrate or (ii) 15% or higher in the presence of 16 mM magnesium sulfate.” RMTA 3 (citing Ex. 1001 at cl. 21). Patent Owner argues that

Claim 22 narrows the scope of claim 21 by ***requiring the further limitation*** that in each respective salt solution, the residual activity of the Factor C expressed in the HEK293 cell must be ***higher*** than either *Limulus polyphemus* Factor C expressed in Sf9 as a host cell or ***higher*** than native *Limulus polyphemus* Factor C. It also maintains the fixed lower limits of recited residual activities in the salt solutions claimed in claim 21 by excluding any Factor C protein exhibiting a residual activity below 10% in the presence of 21 mM sodium citrate or below 15% in the presence of 16 mM magnesium sulfate.

Id.

Petitioner does not argue that substitute claim 22 enlarges the scope of original claim 21. RMTA Opp. 3 (acknowledging that the “inverted negative limitations” in substitute claim 22 “may resolve the broadened scope of PO’s first amended claim 22”), 6 (asserting that “revised claim 22 covers the same . . . range of Factor C protein residual activities as claim 21”).

Based on the above, we find that substitute claim 22 does not enlarge the scope of claim 21.

4. New Matter and Written Description Support in Priority Applications

A motion to amend may not introduce new subject matter. 35 U.S.C. § 316(d)(3); 37 C.F.R. § 42.121(a)(2)(ii). “New matter is any addition to the claims without support in the original disclosure. Normally, a claim element without support in the original disclosure (i.e., the application as originally filed) merits a rejection under 35 U.S.C. § 112 for lack of written description support.” *Lectrosonics*, Paper 15 at 7 (citation omitted). Thus, the Board requires that a motion to amend set forth, for each proposed substitute claim, “written description support in the originally filed disclosure of the subject patent . . . and . . . in an earlier filed disclosure . . . for which benefit of the filing date of the earlier disclosure is sought.” *Id.* (citing 37 C.F.R. § 42.121(b)(1), (2)). “[T]he motion must set forth written description support for each proposed substitute claim as a whole, and not just the features added by the amendment.” *Id.* at 8.

Patent Owner argues that substitute claim 22 “does not introduce new subject matter but is instead supported by, not only the ’318 Patent specification but also the priority ’767 Application.” RMTA 4. Patent Owner cites to substantially similar evidence it cited in its Patent Owner Response and Sur-reply to support adequate written description of challenged claim 21. RMTA 4–7.¹⁵ Patent Owner further points to

¹⁵ Patent Owner cites to the specification of the ’318 patent rather than the ’767 application, but asserts that because “Petitioner concedes the ’318 Patent specification and the ’767 Application specification are identical,” “[c]itations to the ’318 Patent . . . necessarily includes statements also presented in the ’767 Application.” RMTA 4, n.2. We note that to meet the requirement of § 42.121(b)(1), “citation should be made to the original disclosure of the application, as filed, rather than to the patent as issued.” *Lectrosonics*, Paper 15 at 8. Likewise, Patent Owner did not address the

additional disclosures in the specification of the '318 patent (and the corresponding disclosures in the '767 application) as support for the amendments in substitute claim 22, in particular disclosures relating to Factor C having higher residual activities in the presence of 21 mM sodium citrate or 16 mM magnesium sulfate *as compared to Factor C expressed in Sf9 cells and/or a native Factor C*. RMTA 4–5 (citing, e.g., Ex. 1001, 3:13–12:11, 4:5–9, 4:21–25, 35:31–38).

However, as discussed above in our analysis of Petitioner's grounds of unpatentability with respect to claim 21, we find that the '767 application does not provide adequate written description support for *L. polyphemus* Factor C protein recombinantly produced from a HEK 293 cell, as recited in that claim. Patent Owner's additional citations to support written description of the amendments in substitute claim 22, which relate to the residual activity of the claimed Factor C protein, do not change our analysis in that regard. In short, because claim 22 continues to recite *L. polyphemus* Factor C protein recombinantly produced from a HEK293 cell, we find that Patent Owner has not shown, by a preponderance of evidence, that substitute claim 22 is supported by the '767 application.

Furthermore, although Patent Owner cites to the specification of the '318 patent for written description support for substitute claim 22, neither Patent Owner nor Petitioner focuses on whether substitute claim 22

intervening application in the priority chain between the '767 application and the application resulting in the '318 patent. Nevertheless, because there is no dispute among the parties that there are no material differences among the disclosures of the applications in the priority chain, Pet. 20–22, we treat Patent Owner's identification of written description support in the '318 patent specification as also identifying analogous disclosures in the relevant applications in the priority chain.

introduced new subject matter to the '386 application, i.e., the application resulting in the '318 patent. For example, neither party discusses changes in the art between December 10, 2013, Patent Owner's asserted priority date, and April 30, 2019, the date of the '386 application, and how such change may have affected the issue of whether the disclosure of the '386 application would have reasonably conveyed to a POSA that the inventors were in possession, as of April 30, 2019, of the HEK293 recombinant *L. polyphemus* Factor C protein recited in substitute claim 22.

Because we agree that whether substitute claim 22 is entitled to an effective filing date of December 10, 2013, is ultimately dispositive for our decision on the Revised Motion to Amend, we turn to Petitioner's unpatentability arguments without deciding whether the disclosures in the '386 application adequately describe the recombinant Factor C protein recited in substitute claim 22.

D. Petitioner's Unpatentability Arguments

Petitioner bears the ultimate burden to show that any proposed substitute claims are unpatentable. 37 C.F.R. § 42.121(d)(2). For reasons similar to those discussed above with respect to original claim 21, we find Petitioner has met its burden to show that proposed substitute claim 22 would have been obvious over the prior art at issue in the two instituted grounds.

First, for the same reasons discussed above with respect to original claim 21, we find that proposed substitute claim 22 is also not entitled to a priority date of December 10, 2013, because the '767 application does not adequately describe the claimed *Limulus polyphemus* Factor C protein recombinantly expressed from a HEK293 cell.

Second, for the same reasons discussed above with respect to original claim 21, Petitioner has shown, by a preponderance of evidence, that a POSA would have been motivated to obtain a HEK293 recombinant *L. polyphemus* Factor C protein, and that, once the sequence of *L. polyphemus* Factor C became available and compared to the sequence of *T. tridentatus* Factor C, a POSA would have reasonably expected such HEK293 recombinant *L. polyphemus* Factor C protein to have “superior property of being less susceptible to inhibition by ions, as exhibited by Factor C of *Tachypleus tridentatus*.” Ex. 1029, 2–5; *see also, e.g.*, Ex. 1002 ¶¶ 176–180.

Patent Owner acknowledges that the ’767 application, of which Mizumura is the publication, discloses that, for *T. tridentatus*, “the expression of Factor C in HEK293 cells resulted in higher residual activity in each of the claimed salt solutions as compared to corresponding (i) Factor C expressed in Sf9 cells and (ii) native Factor C,” and also “did not have a residual activity less than 10% in the presence of 21 mM sodium citrate or . . . less than 15% in the presence of 16 mM magnesium sulfate.” RMTA 4–7. We therefore find Petitioner has established, by a preponderance of evidence that a POSA would have had a reasonable expectation of success that the HEK293 recombinant *L. polyphemus* Factor C protein suggested by the combination of (1) Mizumura and (2) ’498 PCT or McClymont would meet the residual activity limitations set forth in substitute claim 22.

Accordingly, for the reasons set forth above, we conclude that the subject matter of proposed substitute claim 22 would have been unpatentable as obvious and deny Patent Owner’s Revised Motion to Amend.

IV. RESPONSE TO DISSENT

We respectfully disagree with the Dissent’s position that we should vacate our Decision on Institution and dismiss the Petition as sanction for Petitioner’s violation of 37 C.F.R. § 42.51(b)(1)(iii). Opinion of Administrative Patent Judge Fitzpatrick, dissenting (“Dissent”).

The Dissent bases its proposed sanction on Petitioner’s failure “to serve the Frohman Declaration (Ex. 2004) on Patent Owner when it filed its Petition, despite that the Frohman Declaration contains relevant information that is inconsistent with a position advanced in the Petition.” Dissent 1–2.¹⁶

The Dissent points to the following statement from the Petition, which argues that challenged claim 21 is not entitled to the asserted priority date of December 10, 2013, because it was not adequately described in the ’767 application:

Without the ability to make or describe the function of any recombinant Factor C protein from the claimed *Limulus polyphemus* species of horseshoe crab—whose gene and amino acid sequence was not yet known or disclosed by 2013—the inventors did not and could not describe ***a single example*** of a *Limulus polyphemus* Factor C protein recombinantly produced via HEK293 cells (or by any other mammalian cell) that falls within the claimed range of residual activity in the presence of the recited ions, let alone across its full scope.

Dissent 3 (citing Pet. 25–26).

The dissent similarly points to the following statement in the Petition, which argues that the ’767 application did not, as of December 10, 2013,

¹⁶ As noted above, *see supra* n.11, Petitioner submitted the Frohman Declaration as part of the ’670 Opposition. Ex. 1048, 3.

enable a POSA to make and use the recombinant *L. polyphemus* Factor C protein recited in claim 21 without undue experimentation:

Reaching the full scope of claim 21 therefore requires an extensive amount of experimentation across multiple fronts: (1) to discover and characterize the gene and amino acid sequence for *Limulus polyphemus* Factor C itself, which was not known as of 2013 (*see* Section IX.B, *supra*), (2) to use this as-yet undiscovered genetic information to recombinantly generate Factor C protein across the full scope of residual activity function characteristic as defined by claim 21.

Id. at 3–4 (citing Pet. 38).

The Dissent suggests that these statements are clearly inconsistent with Professor Frohman’s testimony in the ’670 Opposition that “there were multiple ways a skilled person could have obtained ‘the coding sequence of the *Limulus* Factor C protein . . . before October 18, 2016,’”; that “the skilled person would have most likely used Rapid Amplification of cDNA Ends (RACE) to obtain the sequence of the cDNA encoding Factor C *from Limulus polyphemus*”; and that “there was no reason to believe that *Limulus polyphemus* Factor C would have been difficult to express after the cDNA sequence had been obtained.” Dissent 4 (citing Ex. 2004 § III; ¶¶ 7, 44) (emphasis omitted).

However, it is not disputed that “there had not been, as of 2013, the full length cDNA sequence for *Limulus polyphemus* Factor C published.” *See, e.g.*, Tr. 48:18–19. Nor is it disputed that there is no example of *Limulus polyphemus* Factor C protein recombinantly produced via HEK293 cells (or by any other mammalian cell) in the ’767 application. Finally, the passages from the Petition quoted above focus on the functional limitations recited in claim 21—i.e., that claim 21 recites not only a HEK293 recombinant *L. polyphemus* Factor C protein, but one with a particular

recited residual activity, which is not addressed by Professor Frohman's testimony.

Thus, there is no clear inconsistency between the quoted testimony from Professor Frohman—which suggests that a POSA *could* have obtained the coding sequence of the *Limulus* Factor C protein before October 18, 2016 using RACE, and then expressed the protein without difficulty—and Petitioner's general position in the first-quoted passage from the Petition that, as of December 10, 2013, the claimed HEK293 recombinant *L. polyphemus* Factor C protein having a particular recited residual activity “[had] not been invented, and thus cannot be described.” *Ariad*, 598 F.3d 1352 (explaining that claims that do not require undue experimentation to make and use may, nevertheless, “have not been invented, and thus cannot be described”).

The quoted testimony from Professor Frohman is likewise not clearly inconsistent with the general position in the second-quoted passage from the Petition, that extensive experimentation would have been needed to first determine the coding sequence of the *Limulus* Factor C protein and then not merely recombinantly express the protein but to “generate Factor C protein across the ***full scope of residual activity function characteristic*** as defined by claim 21.” Pet. 42 (emphasis added).

The Dissent highlights our determination in the Discovery Order that “[t]he Frohman Declaration ‘is inconsistent with Petitioner's position in the Petition that an ordinarily skilled artisan would not expect experimental protocols for producing recombinant *T. tridentatus* Factor C proteins in HEK293 cells ‘to yield recombinant proteins in soluble and functional form from a different species of crab’ such as *Limulus polyphemus*.’” Dissent 3 (citing Paper 17, 8). We do not disagree that there are statements in the

Frohman Declaration that at least appear to be inconsistent with specific statements in the Petition. *See, e.g.*, Paper 17, 7–9. However, we do not find these statements to be so inconsistent with arguments in the Petition to warrant vacating the Institution Decision and dismissing the Petition as a discovery sanction.

The Dissent acknowledges that Dr. Frohman’s testimony is directed towards a later time frame, October 18, 2016, rather than Patent Owner’s claimed priority date of December 10, 2013. Dissent 4. The Dissent cites to our explanation in the Discovery Order that the Frohman Declaration may nevertheless be inconsistent because the Petitioner took the position in the Petition that its priority arguments with respect to the ’767 application are representative for all other applications in the priority chain, which included later applications. *Id.* (citing Paper 17, 9). However, it is now clear, at the conclusion of the proceeding, that the parties’ priority arguments focus exclusively on whether the challenged claims are enabled and described by the December 10, 2013, filing date of the ’767 application.

We find vacating the Institution Decision and dismissing the Petition to be particularly unwarranted in this case because (1) the sanction would be issued *sua sponte*, at a late stage of the proceeding, without any showing of prejudice to Patent Owner;¹⁷ (2) there has been no apparent consideration of the efficacy of lesser sanctions;¹⁸ (3) the Board and the parties have been aware of the issues with respect to the ’670 Opposition and the Frohman

¹⁷ Patent Owner deposed Petitioner’s expert, Dr. Jain, extensively on the Frohman Declaration. *See, e.g.*, Ex. 1065, 64:22–87:20.

¹⁸ The Dissent asserts that “the majority offer no insight on what would be an appropriate, non ‘*sua sponte*,’ process for resolving this issue.” Dissent 5. These procedures, however, are set forth in 37 C.F.R. §§ 42.11 and 42.12.

Declaration since the earliest stages of this proceeding, including during discretionary denial briefing in front of then-Acting Director Stewart (Papers 6, 8, 9), and there were no prior indication to Petitioner that its discovery shortcomings could result in the dismissal of the Petition;¹⁹ (4) as discussed above, Patent Owner has made statements in its other patent applications that are more directly contradictory to positions it has taken in this proceeding; and (5) Petitioner has made non-frivolous arguments as to why the Opponent's position in the '670 Opposition is not contradictory to the position it has taken in this proceeding (*see, e.g.*, Paper 13).²⁰

Finally, the dissent asserts that "Petitioner's failure to [serve the Frohman Declaration with its Petition] particularly troubling because Petitioner attempted to keep its relationship to the Frohman Declaration secret." Dissent 5. It is not disputed that the EPO permits parties to file patent oppositions anonymously. For the reasons set forth in the Discovery Order, the majority also determined that whether Petitioner initiated the '670

¹⁹ Then-Acting Director Stewart determined that "discretionary denial of institution is not appropriate in [this] proceeding[]" and referred it to the Board for "merits and other non-discretionary considerations." Paper 9, 2. In our Institution Decision, we noted that, "even if we were to take the Frohman Declaration into account, we find that Petitioner has established a reasonable likelihood of success that the '767 application did not enable an ordinarily skilled artisan to make and use the invention of the challenged claim without undue experimentation." Inst. Dec. 28–29.

²⁰ This is not similar to the situation in the *Revvo* line of cases. *Revvo Techs., Inc. v. Cerebrum Sensor Techs., Inc.*, IPR2025-00632, Paper 20 (Nov. 3, 2025) (precedential). In *Revvo*, Petitioner advanced different claim construction positions in litigating the same patent in front of the Board and the district court. *Id.* Here, neither party suggests that the '670 Opposition is a related matter. *See supra* Section I.C. Likewise, we do not find the Frohman Declaration to be necessarily inconsistent with Petitioner's core positions in this case.

Opposition is more properly the province of additional, rather than routine, discovery. Paper 17, 4–5. Patent Owner subsequently filed a Motion to Compel Additional Discovery, after which Petitioner confirmed that it was the party behind the '670 Opposition, which resolved the discovery dispute. Paper 29.

V. CONCLUSION

Based on the information presented, we conclude that Petitioner has demonstrated by a preponderance of evidence that claim 21 is unpatentable. We deny Patent Owner's Revised Contingent Motion to Amend.

In summary:

Claims	35 U.S.C. §	Reference(s)/ Basis	Claims Shown Unpatentable	Claims Not Shown Unpatentable
21	103	Mizumura, '498 PCT	21	
21	103	Mizumura, McClymont	21	
Overall Outcome			21	

Motion to Amend Outcome	Claim(s)
Original claims Cancelled by Amendment	
Substitute Claims Proposed in the Amendment	22
Substitute Claims: Motion to Amend Granted	
Substitute Claims: Motion to Amend Denied	22
Substitute Claims: Not reached	

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has shown, by a preponderance of the evidence, that claim 21 of U.S. Patent No. 11,236,318 B2 is unpatentable;

FURTHER ORDERED that Patent Owner's Revised Contingent Motion to Amend is denied; and

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

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

FITZPATRICK, *Administrative Patent Judge*, dissenting.

I respectfully dissent from the majority's Final Written Decision because I would not reach any final decision on the merits. Instead, I would vacate our Decision on Institution (Paper 14) and dismiss the Petition (Paper 2) on account of Petitioner's violation of 37 C.F.R. § 42.51(b)(1)(iii).

That Rule states:

Unless previously served, a party must serve relevant information that is inconsistent with a position advanced by the party during the proceeding concurrent with the filing of the documents or things that contains the inconsistency. This requirement does not make discoverable anything otherwise protected by legally recognized privileges such as attorney-client or attorney work product. This requirement extends to inventors,

corporate officers, and persons involved in the preparation or filing of the documents or things.

37 C.F.R. § 42.51(b)(1)(iii). “Routine discovery under 37 C.F.R. § 42.51(b)(1)(iii) is narrowly directed to specific information known to the responding party to be inconsistent with a position advanced by that party in the proceeding, and not broadly directed to any subject area in general within which the requesting party hopes to discover such inconsistent information.” *Garmin Int’l, Inc. v. Cuozzo Speed Techs. LLC*, No. IPR2012-00001, Paper 26, 4 (March 5, 2013) (precedential) (“*Garmin*”).

Petitioner failed to serve the Frohman Declaration (Ex. 2004) on Patent Owner when it filed its Petition, despite that the Frohman Declaration contains relevant information that is inconsistent with a position advanced in the Petition. The Frohman Declaration was submitted to the European Patent Office as part of an anonymously filed Opposition to Patent Owner’s European Patent No. 3530670 (“the ’670 Opposition”). *See* Ex. 2006, at 2–3 (Notice of Opposition identifying “**D8**: Declaration of Professor Frohman” as a document “relied upon”).

On August 8, 2025, Patent Owner filed a Motion to Compel in this proceeding. Paper 12. The Motion sought two things from Petitioner: (1) “to confirm whether it initiated the [’670] Opposition” in Europe and (2) to “produce any other relevant information of which it is aware that is inconsistent with a position it advanced in IPR2025-00440.” Paper 12, at 1. In a September 30, 2025, Order, the Board granted the latter and, over a dissent, denied the former. Paper 17.

At the time of the September 30, 2025, Order, it was not established that Petitioner had commissioned the Frohman Declaration or that Petitioner had requested the ’670 Opposition. Those are now undisputed facts of

record. *See* Paper 31 (“On December 19, 2025, Patent Owner informed the Board that Petitioner has confirmed that Petitioner is ‘the party behind the European Opposition proceeding.’” (quoting Ex. 3004)).

It is a fact that the Frohman Declaration was known to Petitioner at the time Petitioner filed its Petition. It is a fact that Petitioner did not serve the Frohman Declaration concurrent with the filing of its Petition. And, the Board has already decided, as a matter of fact, that the Frohman Declaration contains information that is inconsistent with a position advanced in the Petition. *See* Paper 17, at 8 (The Frohman Declaration “is inconsistent with Petitioner’s position in the Petition that an ordinarily skilled artisan would not expect experimental protocols for producing recombinant *T. tridentatus* Factor C proteins in HEK293 cells ‘to yield recombinant proteins in soluble and functional form from a different species of crab’ such as *Limulus polyphemus*.” (quoting Pet. 24)). It clearly does.

In asserting a lack of written description for priority purposes, the Petition argues the following:

Without the ability to make or describe the function of any recombinant Factor C protein from the claimed *Limulus polyphemus* species of horseshoe crab—whose gene and amino acid sequence was not yet known or disclosed by 2013—the inventors did not and could not describe ***a single example*** of a *Limulus polyphemus* Factor C protein recombinantly produced via HEK293 cells (or by any other mammalian cell) that falls within the claimed range of residual activity in the presence of the recited ions, let alone across its full scope.

Pet. 25–26 (citing Ex. 1002 ¶¶69–70, 87). Similarly, in asserting a lack of enablement for priority purposes, the Petition argues the following:

Reaching the full scope of claim 21 therefore requires an extensive amount of experimentation across multiple fronts: (1) to discover and characterize the gene and amino acid sequence

for *Limulus polyphemus* Factor C itself, which was not known as of 2013 (*see* Section IX.B, *supra*), (2) to use this as-yet undiscovered genetic information to recombinantly generate Factor C protein across the full scope of residual activity function characteristic as defined by claim 21.

Pet. 38 (citing Ex. 1002 ¶135).

In contrast to the arguments quoted above, Professor Frohman testified that there were multiple ways a skilled person could have obtained **“the coding sequence of the *Limulus* Factor C protein . . . before October 18, 2016.”** Ex. 2004 § III. For example, Professor Frohman testified that “the skilled person would have most likely used Rapid Amplification of cDNA Ends (RACE) to obtain the sequence of the cDNA encoding Factor C *from Limulus polyphemus*.” *Id.* ¶7. Professor Frohman further testified that there was no reason to believe that *Limulus polyphemus* Factor C would have been difficult to express after the cDNA sequence had been obtained. *Id.* ¶44.

Although Professor Frohman testified as to the skill in the art as of October 18, 2016 (*see id.* ¶3), his testimony nonetheless is inconsistent with Petitioner’s arguments quoted above. As explained in our September 30, 2025, Order:

Petitioner took the position in the Petition that the challenged claim is entitled to an effective filing date no earlier than April 30, 2019, the ’318 patent’s actual filing date. Pet. 42. Petitioner also took the position that its arguments with respect to the ’767 Application [are] representative, and that, “[i]f the representative ’767 Application fails to describe and enable claim 21, . . . all other applications in the priority chain fail for the same reasons.” *Id.* at 22 (emphasis added). Thus, Petitioner’s arguments regarding written description and enablement do not appear to be limited to the 2013 timeframe.

Paper 17, at 9.

Petitioner should have served the Frohman Declaration with its Petition. I find Petitioner's failure to do so particularly troubling because Petitioner attempted to keep its relationship to the Frohman Declaration secret.

As a sanction for Petitioner's violation of 37 C.F.R. § 42.51(b)(1)(iii), I would vacate the Decision on Institution (Paper 14) and dismiss the Petition (Paper 2).

The majority state that such a sanction is unwarranted here, in part, because the sanction "would be issued *sua sponte*, at a late stage of the proceeding, without any showing of prejudice by Patent Owner." *Supra*. However, Patent Owner first brought attention to this issue in its first Motion to Compel, which was filed over a month before the case was instituted. Paper 12. The prejudice is the institution. That institution was prejudicial became clear only upon Petitioner admitting, months later, that it was the party that had requested the '670 Opposition (and thus had commissioned and submitted the Frohman Declaration to the EPO). Ex. 3004. Further, the majority offer no insight as to what would be an appropriate, non "*sua sponte*," process for resolving this issue *that a majority of this panel would support*.

The majority point out that Patent Owner itself has made inconsistent statements (admissions) in an unrelated patent application. This is true and quite troubling. Indeed, I am *certain* that the majority's determination that claim 21 of the '318 patent is unpatentable based, in part, on those admissions is *correct*. The ends, however, do not justify the means.

Finally, the majority note that "Petitioner has made non-frivolous arguments as to why [Petitioner]'s position in the '670 Opposition is not contradictory to the position it has taken in this proceeding." *Supra*. I do

not know to which arguments the majority is referring. It suffices to state, however, that such arguments, even if non-frivolous, were not persuasive. Paper 17.

It is a matter of record that Petitioner violated 37 C.F.R. § 42.51(b)(1)(iii). Paper 17. There must be some meaningful repercussion for violation of a discovery obligation. Had I known, prior to institution, that Petitioner was the party who presented the Frohman Declaration to the EPO (which document Petitioner did not serve with its Petition), I would not have agreed with instituted this proceeding. Thus, I believe that vacating our Decision on Institution and dismissing the Petition would be appropriate here.

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