

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CHARLES RIVER LABORATORIES, INC.,
Petitioner,

v.

SEIKAGAKU CORPORATION,
Patent Owner.

Case No. PGR2025-00023

Patent No. 11,959,109

PATENT OWNER SUR-REPLY

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I. INTRODUCTION

Patent Owner Seikagaku Corp. (“PO”) submits this Sur-Reply to Petitioner Charles River Laboratories’ Reply to Patent Owner’s Response.

Petitioner relies entirely on attorney argument in its Reply even though its declarant, Dr. Siddhartha Jain failed to consider the vast majority of the references illustrating the wealth of general knowledge in the art concerning Factor C, Factor B, and Pro-clotting enzyme and discussed in Patent Owner’s Response (“POR”). But attorney argument cannot undermine substantive expert testimony. *See Parkervision, Inc. v. Vidal*, 88 F.4th 969, 982 (Fed. Cir. 2023). Accordingly, Patent Owner’s evidence concerning the wealth of scientific knowledge available to a person of ordinary skill in the art (“POSA”), and the conclusions a POSA would draw from that knowledge provided via its declarant Dr. Brian C. Schaefer stand un rebutted.

Petitioner’s complaints of improper burden-shifting are unfounded. PO provided argument and ample evidence that claims 1-9 of the ’109 patent are entitled to claim the benefit of the December 10, 2013 filing date of the ’767 Application under 35 U.S.C. § 120. This shifted the burden of production back to Petitioner to prove the ’629 publication is prior art. *Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1380 (Fed. Cir. 2015). The burden of proving unpatentability is always on the petitioner. *Id.* at 1378-79.

Petitioner would like this Board to ignore, as Dr. Jain did, the extensive knowledge concerning the sequences, structures, and functions of Factor C, Factor B, and Pro-clotting enzyme and instead draw conclusions based solely on the lack of sequences and working examples. That would be legal error. Written description and enablement must be evaluated from the perspective of a POSA and in the context of what is already known in the field. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (*en banc*); *Amgen Inc. v. Sanofi*, 598 U.S. 594, 612 (2023). The context here demonstrates the '767 Application provides §112 support for the Challenged Claims.

Petitioner has not met its burden to show the '629 publication is prior art, and the Petition should be denied.

II. PETITIONER'S INCONSISTENT POSITIONS UNDERCUT ITS CREDIBILITY

Petitioner confirmed it initiated the Opposition proceeding against PO's European Patent No. 3530670 ("Opposition"), but only after PO filed two motions to compel additional discovery (Paper Nos. 12, 23) and its POR (Paper No. 26). EX3003. The reason for Petitioner's initial refusal and delay is clear: it cannot reconcile the positions it has taken in the Opposition and before this Board.

As discussed in PO's Response, the arguments and evidence concerning what the '767 Application describes and enables with respect to *Limulus polyphemus*

Factor C Petitioner presented in the Opposition were inconsistent—and often completely at odds—with Petitioner’s arguments and Dr. Jain’s testimony here. *See* Paper No. 17 at 8-12, 14; *see also* POR at 80-90; EX2006 ¶¶48-61, 93-100, 144, 146, 155, 174. Another example of Petitioner’s contradictory positions is its newfound reliance on the ’498 PCT as evidence of technical challenges in the field when it *criticized those same statements* as “very generic and entirely unsupported” and “*factually incorrect*” in the Opposition. *Compare* Reply at 5-7 (quoting EX1005 ¶12) *with* EX2006 ¶¶34-35, 35 n.2, 75 (also discussing EX1005 ¶12)¹ (emphasis added).

Petitioner previously argued to the Board that “no contradiction exists” between the Opposition and this proceeding because the patents at issue “are in different patent families, have different priority dates, and have different specifications.” Paper No. 8 at 11. While factually correct, these differences cannot justify Petitioner’s inconsistent descriptions of the same references—the ’767 Application and the ’498 PCT—in the Opposition and in this proceeding. Notably, Petitioner does not even *attempt* to reconcile any of the numerous inconsistencies between the Opposition and this proceeding in its Reply. Petitioner also makes no

¹ The opposed patent was published as the WO 2018/074498, *i.e.*, the ’498 PCT.

EX2006 ¶ 6.

attempt to explain why its arguments concerning *Limulus polyphemus* Factor C from the Opposition are not equally applicable to cloning and expressing Factor B and Pro-clotting enzyme from that species. PO's evidence that they are equally applicable is therefore un rebutted.

The Board should reject Petitioner's gamesmanship and look askance at its arguments and evidence here. *See Provepharm Inc. v. Wista Lab'ys Ltd.*, No. IPR2018-00323, 2019 WL 2865314, at *15 (P.T.A.B. July 2, 2019) (noting that Petitioner's contradictory statements before the EPO were "strong evidence" undercutting Petitioner's arguments to the PTAB and "at the very least... significantly weaken and undermine the credibility of Petitioner's case, as well as the credibility" of Petitioner's expert which was "also in direct contradiction to Petitioner's earlier assertions."").

Ignoring the blatant contradictions in its own positions, Petitioner attempts to manufacture inconsistencies in PO's positions. Petitioner relies on "for the first time" statements in the '498 PCT as evidence of insufficient written description and enablement support. Reply at 4, 6-7. However, those statements are irrelevant to written description and not probative of enablement.

Actual possession or reduction to practice is not relevant to the written description inquiry, *Ariad*, 598 F.3d at 1352, but even if the Board considers those statements at face value, they do **not** demonstrate the inventors struggled for three

years to accomplish mammalian expression of the proteins in the Challenged Claims. Petitioner's conclusion is based on the unsound *assumption* that the '498 PCT application was filed immediately after completing preliminary experimental work. However, nothing in the '498 PCT supports this assumption, and there is no requirement that inventors must file a patent application immediately upon an actual reduction to practice and not before. *See BASF Plant Sci., LP v. Commonwealth Sci. & Indus. Rsch. Org.*, 28 F.4th 1247, 1267 (Fed. Cir. 2022) ("Because actual reduction to practice is not a requirement of possession, delay in actual production here does not negate constructive possession at the time of filing."). Nor do the statements in the '498 PCT establish lack of enablement of the Challenged Claims as of December 2013 because PO's evidence that the techniques described in the '498 PCT and the '767 Application were standard in the field well before December 2013 is uncontested.² EX2062 ¶¶139-140, 158-159.

Further, PO's arguments have been consistent across jurisdictions. In the Opposition, PO argued "[t]here is no suggestion in the prior art that recombinant LpFC [*Limulus polyphemus* Factor C] would have a higher activity than recombinant

² Contrary to Petitioner's assertion, PO is not trying to "have it both ways" by relying on the prior art to enable the Challenged Claims. Reply at 7, n.2. PO argues the '767 Application enables the Challenged Claims. *See* POR at 65-66, 69-74.

TtFC [*Tachypleus tridentatus* Factor C]. Thus, the subject matter of claim 1 is not obvious.” EX1043 ¶50; *see also id.* ¶52 (“there were no reasons to speculate that LpFC would behave better than TtFC in a recombinant system”) and ¶59 (“Prior to the effective filing date, it was known that native LpFC was ‘indistinguishable’ from native TtFC”). That is entirely **consistent** with PO’s argument here that a POSA understood *Limulus polyphemus* Factor C protein would function similarly to *Tachypleus tridentatus* Factor C. *See, e.g.*, POR at 46, 50-52.

Petitioner’s own description of PO’s arguments concerning the ’767 Application in the Opposition also reflect PO’s consistent positions across jurisdictions. EX2006 ¶¶50-55, 60-61 (discussing D1, the ’767 Application and PO’s arguments concerning D1). For example, Petitioner noted that PO argued to the USPTO that “the skilled person reading the description of [the ’767 Application] would not only be able to produce a *Limulus* Factor C without undue burden, but that they would further expect the invention of [the ’767 Application] to ‘*also work when Factor C is the Factor C of Limulus Polyphemus.*’” EX2006 ¶50 (emphasis original). Petitioner agreed with PO in the Opposition. *Id.* ¶¶54-55. Petitioner acknowledged that PO “believe[s] ‘*in view of the guidance in the specification; the high level of skill in the art; and the existing knowledge in the art, a person skilled in the art would readily be able to generate and use the polypeptides that are*

encompassed by the claims’, including a *Limulus* Factor C.” *Id.* ¶53 (emphasis original).

III. THE CHALLENGED CLAIMS ARE ENTITLED TO A DECEMBER 2013 PRIORITY DATE

Petitioner conspicuously failed to address, much less refute, the extent of general knowledge and information in the art concerning the sequences, structures, and functions of Factor C, Factor B, and Pro-clotting enzyme. *See* POR at 5-17, 49-54. That includes the known functional interchangeability across species of these proteins in the coagulation cascade. *Id.* at 17-19, 54-57. Petitioner acknowledged functional interchangeability was the “underlying assumption” in the field outside of this proceeding in a publication. *Id.* at 56 (citing EX2054 at 3). PO’s expert Dr. Schaefer’s opinions concerning the conclusions a POSA would draw from this wealth of knowledge and information stand un rebutted. *See, e.g.*, EX2062 ¶¶ 112, 121, 124-135, 167-168.

Petitioner also made no attempt to distinguish the cases cited by PO and urges the Board to impose requirements for written description and enablement based on non-analogous cases. The Board should decline to do so.

A. The Specification Demonstrates Possession

Petitioner’s arguments for lack of written description focus almost exclusively on an alleged lack of actual possession of the recited recombinant proteins other than

those from *Tachypleus tridentatus* based on the absence of working examples and sequence information in the '767 Application. Reply at 12-13.

1. Written description does not demand working examples

“[T]he written description requirement does not demand either examples or an actual reduction to practice.” *Ariad*, 598 F.3d at 1352. Petitioner concedes that working examples are not required, arguing that an absence of examples can support a finding of no written description. Reply at 12. However, the only case cited by Petitioner for this premise, *Brita v. ITC*, is inapposite. *Id.* In *Brita*, the specification taught that carbon-block filters were unique and disparaged the non-carbon-block filters recited in the claims at issue. *Brita LP v. Int’l Trade Comm’n*, 156 F.4th 1325, 1332-33 (Fed. Cir. 2025). The claims also required the filters to meet a multi-variable performance factor which was a “complex task with unpredictable challenges.” *Id.* at 1333-34.

In contrast, the '767 Application contains no such statements regarding uniqueness or disparagement of proteins from a particular horseshoe crab species. To the contrary, the '767 Application expressly states that, although *Tachypleus tridentatus* is preferred, proteins derived from any of the four species of horseshoe crab are part of the invention. EX1017 at 40, 58. And rather than being a complex and unpredictable task, practicing the recited method is a straightforward use of

routine “boilerplate” techniques. EX2062 ¶¶94-95; EX2004 ¶¶40-47; EX1067 at 44-46, 104; EX1068 at 282-283.

Petitioner has not shown that the absence of working examples supports finding no written description here.

2. Written description does not require reciting sequences

Petitioner invites the Board to commit legal error by requiring sequences to be recited in the specification or published in their complete form for written description. Reply at 14-17. Written description does not require the specification to recite or incorporate sequence information by reference. *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1368 (Fed. Cir. 2006); *Ariad*, 598 F.3d at 1352 (“The [written description] doctrine never created a heightened requirement to provide a nucleotide-by-nucleotide recitation of the entire genus of claimed genetic material”); *Capon v. Eshhar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005) (“When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh.”); *see also* POR at 38-39 (discussing additional cases).

Instead of distinguishing the cases cited by PO, Petitioner instead attempts to undercut the significance of the sequence data analyzed by Dr. Schaefer in various ways. Reply at 14-15. First, Petitioner wrongly characterizes that data as “bulk transcriptome data for the entire *Limulus polyphemus* horseshoe crab.” *Id.* at 14. The deposit Dr. Schaefer analyzed was the transcriptome from *Limulus polyphemus*

amoebocytes. EX2062 ¶¶35, 69; EX2072. This data set contains cDNA sequences only, isolated from the very cell type in which Factor C, Factor B, and Pro-clotting enzyme are present. The narrowness of the data set significantly reduces the sequence analysis needed to reassemble the protein sequences as compared to starting from whole genome data. EX2062 ¶79.

Petitioner quibbles that Dr. Schaefer did not verify the publication date of the BioProject and sequence deposits he analyzed. However, Petitioner did not object to admissibility or move to exclude the relevant exhibits or Dr. Schaefer's opinions based on those exhibits. 37 C.F.R. §42.64. Any objection to the publication date is waived. Further, Petitioner ignores that assembling the sequences from data deposits is only one of three different approaches to arrive at the *Limulus polyphemus* sequences. EX2062 ¶¶76-92; EX1067 at 106-107, 109-110. Professor Frohman, Petitioner's expert in the Opposition, testified similarly with respect to Factor C, and Petitioner has not rebutted Dr. Schaefer's testimony that Professor Frohman's opinions would apply equally to all of the proteins in question as of December 2013. EX2062 ¶¶76, 80.

Second, Petitioner accuses Dr. Schaefer of using impermissible hindsight to make predictions about protein function. Reply at 15. Not so. Petitioner mischaracterizes Dr. Schaefer's work and testimony. Dr. Schaefer used the *T. tridentatus* cDNA sequences disclosed in the '767 Application to identify the

corresponding sequences in the *Limulus polyphemus* transcriptome data to verify that nearly complete sequence of Factor C and complete sequences of Factor B and Pro-clotting enzyme could be reassembled. EX2062 ¶¶70-72. The testimony cited by Petitioner concerned a **different** analysis—a Clustal alignment that identified the few non-conservative substitutions in the *Limulus polyphemus* proteins compared to two other species. *Id.* ¶115; EX1067 at 110-111. The purpose of this alignment was to confirm the reports in the art that the protein sequences are highly similar overall. *See* EX2062 ¶¶29-34, 113-115. Dr. Schaefer’s opinions were not based on hindsight. He expressly opined that a POSA would understand the functional identity and interchangeability of Factor C across species even without the sequence analyses. *Id.* ¶¶121-126.

Third, Petitioner criticizes Dr. Schaefer for not actually reconstructing the cDNA sequences of Factor C, Factor B, and Pro-clotting enzyme from the transcriptome data deposit. *See* Reply at 15, 17. This is a red herring. Dr. Schaefer explained that reconstructing the full sequence from sequence deposits is not what a POSA would do with the information. EX1067 at 102-104; EX1068 at 264-266. Rather, a POSA would use the sequences to design PCR primers and amplify the cDNA from a sample. *Id.*; *see also* EX2004 ¶29; EX2006 ¶¶41-42. The sequence information in the ’767 Application allowed a POSA to do the same. EX2062 ¶¶80, 84-88; EX2004 ¶¶6-7, 10-12, 14-26, 30-33. Dr. Schaefer’s testimony demonstrates

that even if the '767 Application had recited the cDNA sequences of the *Limulus polyphemus* proteins, a POSA would still need to undertake the same routine experiments to practice the Challenged Claims—which are directed to *proteins*, not sequences.

Petitioner asserts the inventors admitted in a different patent that the Factor B sequences from *Carcinoscorpius rotundicauda* and *Tachypleus gigas* were not known. Reply at 16-17 (quoting EX1070). However, Petitioner omits the end of the quoted sentence: “however, those ordinarily skilled in the art can understand that the technology of the present invention is also applicable to the polypeptides of these factors B.” EX1070 at 10:15-19. The complete sentence is wholly consistent with Patent Owner’s arguments here.

3. Patent Owner is not improperly gap-filling

The preponderance of the evidence indicates that the sequence deposits Dr. Schaefer analyzed are accessible literature sources known to POSAs that covered nearly the entire cDNA sequence of Factor C, and the entire cDNA sequences of Factor B, and Pro-clotting enzyme of *Limulus polyphemus*. EX2062 ¶¶35-36, 68-73; EX2004 ¶¶6, 18-21; EX1064 at 25, 70; EX1067 at 96-97; EX1068 at 264-266. Further, in the Opposition, Petitioner argued that “it is a matter of routine practice for a person skilled in the art to determine the sequence of a known protein” and could have been accomplished “without the need for any inventive skill.” EX2006

¶¶59, 98-99. Therefore, neither recitation nor incorporation by reference of nucleotide-by-nucleotide information is required for written description here. *Falko-Gunter*, 448 F.3d at 1368-69.

Nonetheless, Petitioner accuses Patent Owner of “improper gap-filling” citing *Novozymes* and *Rivera*. Reply at 13, 21. But those decisions turned on different facts. In *Novozymes*, the specification did not describe any mutations that would yield variants with increased thermostability as recited by the claims. *Novozymes A/S v. DuPont Nutrition Biosci. APS*, 723 F.3d 1336, 1350 (Fed. Cir. 2013). And in *Rivera*, there was no mention at all of the disputed claim limitation in the specification at issue there. *Rivera v. Int’l Trade Comm’n*, 857 F.3d 1315, 1322 (Fed. Cir. 2017) (“nothing in the ’320 patent disclosure indicates the possibility of a cartridge with an integrated filter”). Thus, these two cases dealt with a lack of *in haec verba* disclosure of the recited claim limitations, thus neither are persuasive.

Here, as Petitioner admitted in the Opposition, “the use of Factor C derived from *Limulus polyphemus* is explicitly disclosed as one of the specific ‘Modes for Carrying out the Invention’” by the ’767 Application. EX2006 ¶¶48, 155. The use of recombinant Factor B and Pro-clotting enzyme from each of the four species of horseshoe crab is also explicitly disclosed. EX2062 ¶¶66, 68, 94-97 (citing EX1017). The specification also discloses combining recombinant Factor C, Factor B, and Pro-clotting enzyme into an endotoxin assay agent. EX1017 at 30, 57

([0044]). Contrary to Petitioner's assertion (Reply at 17), expression in the same or different types of mammalian host cells is also described. EX1017 at 53-54 ([0038]), 62-63 ([0056]-[0057]), 67 ([0068]).

4. Mammalian expression of Factor B and Pro-clotting enzyme is expressly described

The '767 Application expressly states that the techniques for expressing Factor C in mammalian cells may be applied to expressing Factor B and Pro-clotting enzyme. EX1017 at 63; EX2062 ¶¶94-97; POR at 37, 40. Petitioner criticizes the *mutatis mutandis* language as “unscientific” and “boilerplate” (Reply at 13, 24), but that does not mean the disclosure is insufficient. The experts agree the phrase informs a POSA that the same procedure disclosed for Factor C can be used to produce Factor B and Pro-clotting enzyme. EX1068 at 277-278, 282-283; EX1065 at 156. Specialized instructions are not necessary to satisfy the written description requirement, particularly where the evidence shows that none were needed. *See Regents of the Univ. of Cal. v. Broad Inst., Inc.*, 136 F.4th 1367, 1383 (Fed. Cir. 2025) (acknowledgings “an indication that no specific instructions or conditions were necessary” could show or establish possession); EX2062 ¶96.

Petitioner argues recombinant protein expression is unpredictable, but its support does not reflect the state of the art as of December 2013 and are therefore irrelevant. First, Petitioner cites a PO patent concerning recombinant expression of

Pro-clotting enzyme. Reply at 19 (citing EX2050). But this 2008 patent publication describes *successful* recombinant expression of active Pro-clotting enzyme in insect cells, which in turn indicates that the protein could be successfully expressed in mammalian cells with routine experimentation. EX2050 at 4, 25 ([0007], [0134]); POR at 71-72.

Second, Petitioner points to a 1997 publication that described difficulties expressing Factor C in COS-1 cells. Reply at 20 (citing EX1026). This was a problem *solved by the inventors* and *excluded* from the scope of the Challenged Claims. POR at 65. Third, Petitioner quotes a statement from a 2017 publication co-authored by inventor Dr. Mizumura that is not in evidence in this proceeding.³ Reply at 20 (citing EX1033); Reply at vi (identifying EX1033 as “reserved”).

Petitioner simply does not respond to PO’s evidence concerning what a POSA would understand and expect from the disclosures of the ’767 Application itself. *See, e.g.,* EX2062 ¶163; EX1068 at 288-290. Tellingly, Petitioner’s highly experienced expert from the Opposition did not foresee any difficulties with

³ The Board should decline to consider evidence that is not in the record. Regardless, the quote is a general statement citing a publication concerning expression of human proteins in yeast, not an admission by Dr. Mizumura concerning the recombinant expression of the proteins at issue.

recombinantly expressing *Limulus* Factor C in view of the '767 Application's disclosures of successful expression of *Tachypleus* Factor C. EX2004 ¶¶44-47; *see also* EX2006 ¶119. Petitioner has not explained why a POSA would draw the opposite conclusion concerning Factor B and Pro-clotting enzyme.

Further, the knowledge in the art was extensive, and considered by Dr. Schaefer, but not by Petitioner's declarant Dr. Jain. EX2062 ¶¶22-47, 94-97; EX1003 ¶12; EX1065 at 17-18. Dr. Jain's uninformed testimony should be given little weight. Patent Owner's evidence establishes sufficient written description of expression of Factor B and Pro-clotting enzyme in mammalian cells. *See BASF*, 28 F.4th at 1266 (affirming verdict of adequate written description based on that POSAs "would have expected that the invention as claimed would work" in canola cells based on the specification's examples using *Arabidopsis* cells and knowledge in the art); *Amgen, Inc. v. Hoechst Marion Roussel*, 314 F.3d 1313, 1335 (Fed. Cir. 2003). Petitioner has failed to show otherwise.

5. The specification discloses a representative species

Petitioner does not respond to PO's evidence that the *Tachypleus tridentatus* proteins disclosed in the '767 Application are representative of the corresponding

proteins of the other three species of crab.⁴ POR at 45-46, 52-54 (citing EX2062 ¶¶ 40, 131-134; EX2094). Petitioner does not respond to Patent Owner’s argument that claim 1 covers as few as 32 potential combinations of ten proteins, and claim 4 covers as few as eight potential combinations of six proteins. POR at 39-45.

Instead, Petitioner makes the circular argument that because there was no actual possession, the ’767 Application cannot disclose a representative species as a matter of law. Reply at 21. Not so. As discussed, Petitioner has not established lack of actual possession or reduction to practice, which is irrelevant in any case. *Falko-Gunter*, 448 F.3d at 1366 (“The Board was correct... not to view as dispositive that [patent owner] had not actually *produced* a [claimed] poxvirus vaccine, because an actual reduction to practice is not required for written description.”) (emphasis original). Further, the ’767 Application expressly describes each component of Claim 1 and how to combine them in the recited method. POR at 32-33; EX1017 at 87-88, 93-95 ([0108]-[0115], [0129]-[0131]).

⁴ In yet another unexplained contradiction, Petitioner advanced a similar argument in the Opposition concerning the representativeness of the *Tachypleus tridentatus* Factor C disclosed in the ’767 Application. EX2006 ¶¶ 49-51 (acknowledging that *Limulus polyphemus* Factor C was encompassed by the claims as granted).

These express disclosures render *In re Ruschig*, *Rivera*, and other “blaze marks” cases inapposite because blaze marks are needed only when the specification *lacks* express disclosure of a sub-genus within a generically described genus. *In re Ruschig*, 379 F.2d 990, 995 (C.C.P.A. 1967); *Rivera*, 857 F.3d at 1322; *BASF*, 28 F.4th at 1265 (distinguishing cases in the “‘blaze mark’ strain of written-description doctrine” where the specification expressly identified canola as a preferred embodiment). Petitioner conceded that the ’767 Application expressly discloses use of proteins from other horseshoe crab species, including *Limulus polyphemus*. See EX2006 ¶119 (“[The ’767 Application]... directly points the skilled person to carry out this method [of recombinant production in mammalian cells] with a Factor C derived from *Limulus polyphemus* species.”). Nor is there agreement here that the art is unpredictable, such that a POSA would need to actually make and test the recited recombinant proteins, unlike in *Novozymes*. 723 F.3d at 1350. To the contrary, in the Opposition, Petitioner agreed with PO that a POSA would extrapolate functional activity and successful expression across species. EX2006 ¶¶102-103, 112, 114 (Petitioner arguing in the Opposition that a POSA would expect recombinant *Limulus* Factor C to exhibit ‘full biological activity’ based on reference D5 reporting recombinant *Carcinoscorpius rotundicauda* Factor C expressed in insect cells was functional).

Petitioner does not dispute that the proteins were well-known and most had been characterized in their native form. POR at 3-15. Thus, the genus of proteins here was “already well explored in the relevant art” as of December 2013 such that the *Tachypleus tridentatus* proteins and results disclosed in the ’767 Application constitute a representative number of species. *Ajinomoto Co., Inc. v. Int’l Trade Comm’n*, 932 F.3d 1342, 1359 (Fed. Cir. 2019) (finding disclosure of four examples of potent promoters a representative number of species for the genus of more potent promoters because the genus was “well explored” in the relevant art at the time of the invention).

Petitioner’s position is based on a proposition that has been ***rejected*** by the Federal Circuit, namely, that disclosure of a single species within a genus categorically fails the written description requirement. *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1123-24 (Fed. Cir. 2004) (discussing cases). Here, the disclosure comprises proteins from one out of a “genus” of four literal species of horseshoe crab. That does not foreclose claims directed to corresponding proteins from other species of horseshoe crab. *Id.* at 1124.

As PO’s evidence establishes, and which Petitioner does not dispute, the structure and function of native Factor C, Factor B, and Pro-clotting enzyme was ***known*** to be similar across the four species and therefore ***predictable***. POR at 46-57; *see also* EX1068 at 69-70. Thus, the ’767 Application’s disclosure of a species

within a very small genus satisfies the written description requirement. *Bilstad*, 386 F.3d at 1125 (noting that unknown embodiments in unpredictable fields are “exceptions to the general rule that disclosure of a species provides sufficient written description support for a later filed claim directed to the genus”). Express disclosure of sequences from other crab species is not necessary to show possession because a POSA would “readily discern that other members of the genus would perform similarly to the disclosed members.” *Id.*; see also *Alcon Rsch. Ltd. v. Barr Lab ’ys, Inc.*, 745 F.3d 1180, 1190-91 (Fed. Cir. 2014) (rejecting argument that disclosure of physical data from only one compound was insufficient to support written description across a range of formulation parameters).

6. A structure-function correlation was known in the art

Petitioner fails to meaningfully respond to PO’s argument that structure, function, and structure-function correlation across proteins and species were known in the art, sufficient to satisfy the written description requirement. POR at 46-57. Petitioner also does not respond to PO’s criticisms of Dr. Jain’s opinions and support concerning the state of the art of recombinant protein expression in December 2013.⁵ POR at 67-69; EX2062 ¶¶147-149. Petitioner’s only response is to argue

⁵ Presumably, Petitioner intended to cite EX1003 ¶¶89-92, not EX1002 on page 22 of its Reply.

counterfactually about *Carcinoscorpius rotundicauda* Factor C, which was known to be expressed but not secreted by COS-1 cells and is outside the scope of the claims. Reply at 21-22.

Petitioner cites a declaration by co-inventor Dr. Mizumura in the '109 patent prosecution history to challenge the representativeness of the disclosed *Tachypleus tridentatus* sequences. Reply at 22. The declaration was submitted to support unexpected results with Factor C. EX1002 at 107, 125-126. It cannot contradict PO's arguments here about Factor B or Pro-clotting enzyme. And it does not support Petitioner regardless. To the contrary, results reported in the declaration **support** PO's extrapolation because it shows that *Tachypleus tridentatus* Factor C and *Limulus polyphemus* Factor C isolated from the intracellular fraction of various mammalian cells were inactive, similar to what had been previously reported for *Carcinoscorpius rotundicauda* Factor C in COS-1 cells. EX1002 at 106-111.

B. The Challenged Claims are Enabled

Petitioner fails to respond to numerous points raised by PO, including that its evidence is outdated or inapposite (POR at 67-69); it failed to come forward with evidence that expressing Factor B and Pro-clotting enzyme in mammalian cells with present a technical challenge (POR at 70-73); the level of routine experimentation in the field is high (POR at 70-75); and Dr. Jain's lack of relevant experience and

misunderstanding of the claims (POR at 76-80).⁶ In sum, Petitioner has failed to meet its burden on enablement. *See Streck Inc. v. Rsch. & Diagnostic Sys., Inc.*, 665 F.3d 1269, 1291-92 (Fed. Cir. 2012) (upholding JMOL of enablement because the evidence established “no undue experimentation would be necessary once the teachings in the patents-in-suit were known” and challenger failed to offer any evidence showing that a POSA could not follow the patent’s teachings to use species of reticulocyte other than those described in the patent).

For example, Petitioner merely reiterates its argument that there were “ample reports of certain mammalian systems not working” (Reply at 23) but only one such report was specific to any of the proteins at issue available as of December 2013: EX1026, which describes the problem the inventors *solved*. Reply at 17-20; *see* POR at 68 (discussing EX1026). Petitioner’s criticisms of the *mutatis mutandis* language in the enablement context (Reply at 24), fall short for the same reasons discussed in Section III.A.4, above with respect to written description. It is well-established that “[t]he specification need not explicitly teach those in the art to make

⁶ Petitioner claims that the “vast majority of PO’s enablement citations” are found at POR 64-65 and focus on EX2004 and EX2006 (Reply at 24), but that is incorrect. Patent Owner addressed enablement at pages 61 through 76, citing many exhibits directly and also indirectly through Dr. Schaefer’s declaration.

and use the invention; the [enablement] requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without ‘undue experimentation.’” *Amgen v. Hoechst Marion*, 314 F.3d at 1334.

Petitioner also relies on *Brita* but that case is inapposite for enablement as it is for written description. The evidence in *Brita* demonstrated differences between the disclosed carbon block filters and other filter media types, and that new technology was needed to create non-carbon-block embodiments. *Brita*, 156 F.4th at 1338-39. Here, the undisputed evidence shows the proteins are *similar* across the four horseshoe crab species and, guided by the ’767 Application, a POSA would only need well-established techniques to practice the claimed method. POR at 64-66; EX1068 at 281-283, 289-290; *see also* EX2006 ¶¶102-103, 112, 114 (Petitioner arguing in the Opposition that a POSA would expect recombinant *Limulus* Factor C to exhibit ‘full biological activity’ based on reference D5 reporting recombinant *Carcinoscorpius rotundicauda* Factor C expressed in insect cells was functional).

Petitioner argues that PO cannot rely on the Frohman Declaration and its Opposition arguments to support enablement because they relate to the state of the art in 2016 and a different patent. Reply at 24. The Board previously found these arguments unpersuasive. Paper No. 17 at 8-9. Further, Petitioner failed to respond to PO’s evidence that the arguments and reasoning would apply equally to Factor B

and Pro-clotting enzyme in 2013. POR at 40-41, 64-66; EX2062 ¶¶76, 94-97, 158-159. Nor has Petitioner identified a change in the state of the art from 2013 to 2016 that could explain its inconsistent positions.

Finally, Petitioner argues the '629 publication does not demonstrate enablement of the full scope of claim 1 as of 2013. Reply at 25. PO has explained that the “full scope” of claim 1 is narrow. POR at 43-45, 53-54. Petitioner does not respond. Nor does Petitioner explain why the *same* disclosures made in December 2013 in the '767 Application are not enabling. POR at 70-74; EX2062 ¶¶156-161.

PO's un rebutted evidence that it would be routine for a POSA to express the three proteins in multiple mammalian cell lines with a reasonable expectation of success in view of the teachings of the '767 Application (*see, e.g.*, EX1068 at 274, 280, 282-283) establish enablement under *Amgen v. Hoechst Marion*. In that case, the Federal Circuit affirmed enablement of claims reciting *inter alia* human erythropoietin (EPO) purified from mammalian cells based on the specification's disclosure of “at least one way of obtaining EPO purified from mammalian cells in culture” and testimony that a skilled artisan “would infer from the COS-1 (monkey) and CHO cell examples that similar outcomes could be expected from other mammalian cells since all mammalian cells produce and secrete hormones like EPO by means of the same fundamental processes.” *Amgen v. Hoechst Marion*, 314 F.3d at 1335; *see also id.* at 1337 (“any challenge which one of ordinary skill in 1984

might have encountered in attempting to make and use the claimed invention using other cultured mammalian cells could be resolved by experimentation falling short of undue.”). Based on the similar evidence presented by both PO and Petitioner in the Opposition, the Board should reach the same conclusion here.

IV. CHALLENGED CLAIMS 2-9 DO NOT STAND OR FALL WITH CLAIM 1

Contrary to Petitioner’s insinuation, PO does not agree that dependent claims 2-9 stand or fall with claim 1. Reply at 26. To the contrary, PO argued that claim 4 in particular requires fewer proteins to practice and limited the species from which those proteins are derived. POR at 30, 45. This narrowing affects at least the representative species aspect of written description and the breadth of the claims and extent of experimentation *Wands* factors for analyzing enablement. POR at 46, 75-76. Thus, PO’s arguments that claim 4 are entitled to claim priority to the ’767 Application are stronger than for the other Challenged Claims.

V. CONCLUSION

The Board should deny the Petition.

Respectfully Submitted,

Dated: April 13, 2026

/s/ Alexander B. Stein
Alexander B. Stein, Reg. No. 71,397

CERTIFICATE OF COMPLIANCE

I, the undersigned, certify that the foregoing Patent Owner Sur-Reply complies with the applicable type-volume limitations of 37 C.F.R. § 42.24(c)(4). Exclusive of the portions exempted by 37 C.F.R. § 42.24(a)(1), this Petition, including footnotes, contains 5,529 words, as counted by the word count function of Microsoft Word. This is less than the limit of 5,600 words as specified by 37 C.F.R. § 42.24(c)(4).

Respectfully Submitted,

Dated: April 13, 2026

/ Alexander B. Stein /
Alexander B. Stein, Reg. No. 71,397

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e)(4), lead counsel for Patent Owner hereby certifies that on April 13, 2026, a copy of this PATENT OWNER SUR-REPLY was served via the email correspondence address of record for Petitioner's counsel of record:

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