

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. IPR2025-00440
Patent No. 11,236,318

**PETITIONER'S OPPOSITION TO PATENT OWNER'S
REVISED CONTINGENT MOTION TO AMEND**

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I. INTRODUCTION

Patent Owner's ("PO's") "revised" amendment creates additional § 112 problems while simultaneously failing to address those rendering original claim 21 unpatentable. Contrary to PO's assertion, PO's new rearrangement of limitations in revised claim 22 suffers from the same written description and enablement deficiencies that plague claim 21 and, in fact, revised claim 22 introduces a new dimension to original claim 21 that finds *even less* support in the '767 Application. As such, revised claim 22 is just as unpatentable as claim 21. Because PO has still failed to remedy—via revised claim 22—the written description and enablement shortcomings of claim 21 for the instant Motion to be considered at all, PO's Revised Contingent Motion to Amend ("RMTA") should be denied.

II. REVISED CLAIM 22 DOES NOT SATISFY THE REQUIREMENTS OF 35 U.S.C. § 316 AND 37 C.F.R. § 42.121

Revised claim 22 fails to satisfy the requirements of 37 C.F.R. § 42.121 because it covers the same unsupported scope as original claim 21 and PO has offered no alternative evidence or explanation as to why this "amended" version addresses or alleviates the unpatentability of claim 21. In fact, as discussed below, revised claim 22 introduces new matter in the form of a claimed relationship between recombinant *Limulus polyphemus* Factor C proteins and two comparator proteins (Sf9-expressed Factor C and native Factor C)—the former being "higher"

than the latter in the presence of certain ion concentrations—that is also neither described nor enabled by the '767 Application. PO's motion should be denied.

A. Revised Claim 22 Still Recites the Unsupported Scope of Original Unpatentable Claim 21

Recognizing the lack of written description and enablement for its broadly and functionally claimed recombinant *Limulus polyphemus* Factor C proteins of claim 21, PO initially abandoned the fixed lower bounds of the claimed residual activity ranges in its first amended claim 22. Paper No. 27, Appx. A (deleting the limitations of “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.”). Having deleted these lower bounds, PO instead opted for a scope of recombinantly produced *Limulus polyphemus* Factor C proteins defined by their residual activity *relative to two comparator proteins* (*L. polyphemus* Factor C protein expressed in a Sf9 cell or a native *L. polyphemus* Factor C protein). *Id.* PO's first amended claim 22 defined the scope of its claimed recombinant proteins as any that had a residual activity that was “higher” than either of these comparator proteins. *Id.* As Petitioner pointed out in its Opposition and the Board recognized in its Preliminary Guidance, this amendment impermissibly *broadened* the scope of claim 22 relative to claim 21 because the residual activity values for these comparators could be lower than the lower end of the broad ranges originally claimed. Paper No. 33, 1-6; Paper No. 34, 5-7.

Now, to address this impermissible broadening, PO imports these lower bounds **back into** revised claim 22 as negative limitations (i.e., explicitly **excluding** from the scope of revised claim 22 any otherwise claimed *Limulus polyphemus* recombinant Factor C protein that has a residual activity **less than** 10% in the presence of 21 mM sodium citrate or 15% in the presence of 16 mM magnesium sulfate). See Paper No. 36, Appx. A. So, revised claim 22’s recitation of “not...less than 10% residual activity” and “not...less than 15% residual activity” is simply an inversion of claim 21’s original limitations 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.”¹

While these inverted negative limitations may resolve the broadened scope of PO’s first amended claim 22, there is no support in the ’767 Application for such additional negative claim limitations and PO points to none. See generally, Paper No. 36. Specifically, the ’767 Application never discusses or describes the purported invention in terms of affirmatively **excluding** *Limulus polyphemus* recombinant Factor C proteins with residual activities “less than” the now claimed upper ranges. The ’767 Application offers no rationale for this exclusion nor ties the 10% or 15% cutoffs to any aspect of the purported invention of recombinant

¹ Emphasis added and internal citations omitted unless noted otherwise.

Limulus polyphemus Factor C proteins with some novel functional property. The **only thing** PO says about these added limitations in its Revised Motion is that they are essentially **the same limitations** as the deleted claim language—that they “maintain[] the fixed **lower limits** of recited residual activities in the salt solutions claimed in claim 21[.]” Paper No. 36, 3-4; *see also, id.* at 15 (characterizing the new negative limitations as “set[ing] a floor for the residual activity”). Per PO’s characterization, these new negative limitations are effectively the same original lower range bounds from claim 21. However, PO admitted that these lower bounds of the claimed residual activity ranges lacked written description support and an enabling disclosure when it did away with them in POs first failed attempt to cure claim 21. PO has reintroduced the problem it originally tried to remove.

In addition, although PO claims to have additionally “narrowed” revised claim 22 by adding “the further narrowing limitation relating to comparator proteins” (Paper No. 36, 3-4), this assertion is incorrect. Recall this “higher than” comparator limitation **broadened** PO’s first claim 22 relative to claim 21. Because either of these comparator proteins could have (and were shown to have)² residual

² Again, the description and lone example in the ’767 Application are **not** of the claimed recombinant *L. polyphemus* Factor C proteins but of the **unclaimed** *Tachypleus tridentatus* species. Still, the examples of Sf9-expressed *T. tridentatus*

activities falling **below** the values in the new negative limitations (i.e., 1% (Sf9) or 3% (native) in the presence of 21 mM sodium citrate or 5% (Sf9) or 10% (native) in the presence of 16 mM magnesium sulfate, *see* EX1001, FIG. 7), and because revised claim 22 excludes any Factor C proteins with residual activities below 10% in 21 mM sodium citrate or 15% in 16mM magnesium sulfate (and thus only includes those Factor C proteins with residual activities at or higher than these

and native *T. tridentatus* Factor C proteins are shown to be very low in the '767

Application. Petitioner does not concede and has explained why such values cannot be extrapolated to residual activities for *L. polyphemus* Factor C proteins. Pet., 23-35; Reply, 8-20. However, to assess the scope of revised claim 22, the low values for Sf9-expressed and native *T. tridentatus* Factor C protein demonstrate that a claim excluding proteins with values of “less than 15%” or “less than 10%” (i.e., revised claim 22) will not be narrower than a claim encompassing proteins with values of “10% or higher” or “15% or higher” (i.e., original claim 21). Put differently, there is nothing suggesting that the comparator proteins will have a residual activity **greater** than 10% in 21 mM sodium citrate or 15% in 16 mM magnesium sulfate such that the scope of Factor C proteins encompassed by revised claim 22 would be **less than** original claim 21. Of course, the uncertainty about these values underscores the § 112 deficiencies of all of these claims.

values) revised claim 22 covers the same unsupported and non-enabled range of Factor C protein residual activities as claim 21. As discussed below, PO's revised claim 22 has solved nothing in terms of the written description or enablement deficiencies of claim 21.

B. PO Fails To Demonstrate Why Revised Claim 22 Finds Written Description Support and an Enabling Disclosure Where Claim 21 Does Not

PO incorrectly characterizes claim 22 as “narrowed” relative to claim 21.³ But in any case PO should explain why claim 22 finds written description support and an enabling disclosure in the '767 Application where original claim 21 did not. PO has failed to do so.

On pages 4-7 of its Motion, PO points to various passages in the '767 Application as alleged “disclosures” supporting revised claim 22 and argues that the revised claim does not add new matter. But PO has already pointed to these same passages as written description support and/or an enabling disclosure for

³ PO repeatedly relies on this misconception of revised claim 22 being “narrowed” relative to original claim 21 to wrongly assert that claim 22 survives Petitioner's priority challenge even if claim 21 does not. *See e.g.*, Paper No. 36, 2 (“This amendment directly responds to that [priority] argument by narrowing the residual activity limitations to overcome the priority date challenge[.]”).

original claim 21. For example, the passages identified at pages 4-5 of PO's RMTA are the same or nearly the same passages as those identified at pages 7-8, 13-14 and 26, n. 4 of the POR. *Compare* Paper No. 36, 4-5, *with* POR, 7-8. But as Petitioner has detailed, none of these passages discuss recombinant *L. polyphemus* Factor C expressed via HEK-293 cells at all. Pet., 2, 25-27.

PO points to Figure 7 of the '767 Application (Paper No. 36, 5-6), which has been cited at length by both parties. *See e.g.*, Pet., 29-30; POR, 8-9. But there is nothing about Figure 7 of the '767 Application that supports or enables revised claim 22 where it was previously insufficient to describe or enable claim 21 (and PO offers no explanation whatsoever for why this would be the case).

Even PO's second declaration from its expert, Dr. Schaefer, relies almost exclusively on his original opinion regarding claim 21. EX2108, ¶¶7, 13. It also relies on the well-tread example and data provided in FIG. 7 which, as noted, PO has already cited at length (unsuccessfully, if this Motion is being considered) as supporting original claim 21. *Compare* POR, 14, *with* EX2108, ¶¶8-9; *compare* POR, 26-27, *with* EX2108, ¶10. Finally, Dr. Schaefer points to a 21-page laundry list of "modes" of the present invention (¶17) provided in the specification of the '767 Application, wherein two such modes refer to a generic Factor C exhibiting a "higher" residual activity in the presence of the two claimed ion concentrations relative to Factor C recombinant expressed in Sf9 cells or a generic native Factor

C. EX2108, ¶11. But this mention of the “higher residual activity” limitation, disjointed from the other features of claim 22 (i.e., expression in HEK293 cells, use of *Limulus polyphemus* Factor C sequences), is insufficient to describe the full scope of that claim. *Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1349-50 (Fed. Cir. 2013) (claim invalid for lacking adequate written description—“While the 2000 application provides formal textual support for each individual limitation recited in the claims...it nowhere describes the actual functioning, thermostable alpha-amylase variants that those limitations together define.”). PO’s reliance on the isolated disclosure of Factor C residual activities that are “higher” than the claimed comparators, decoupled from the now-claimed negative limitations, the HEK-293 recombinant system, and the *Limulus polyphemus* species for recombinant production does not constitute the requisite disclosure of an “integrated whole” under *Novozymes*. *Id.* at 1349-50. Finally, Dr. Schaefer cites his original declaration (EX2038) as support for the idea that *L. polyphemus* and *T. tridentatus* horseshoe crabs are “functionally interchangeable”. EX2108, ¶13. But, as discussed below, this argument was refuted in Petitioner’s Reply and in any case adds nothing to the disclosure of revised claim 22 that was not already considered—and rejected—as to claim 21.

PO dismissed the fact that the ’767 Application discusses residual activity measurements and values for the unclaimed *Tachypleus tridentatus* horseshoe crab

and not the claimed *Limulus polyphemus* horseshoe crab because “a POSA would have understood Factor C proteins are highly conserved among horseshoe crab species such that Factor C from *Limulus polyphemus* would also exhibit the claimed residual activity limitations.” Paper No. 36, 7, 10-12. However, this is the **exact same** argument that PO makes in trying to maintain that claim 21 should be entitled to claim priority to December 13, 2013. POR, 17-21. If revised claim 22 is being considered for patentability, however, it is because this Board has **rejected** the sufficiency of the “highly conserved” argument for written description and/or enablement purposes. As Petitioner detailed in the Petition and Reply, the evidence of record is such that a POSA would understand Factor C proteins across different species of horseshoe crab could behave **differently** in the context of specific functional assays such as measurements of residual activity. Pet., 23-35; Reply, 11-20. The evidence offered by PO itself undermines its “functional interchangeability” argument. EX2035, 21, FIG. 1, 6; EX2049, 4, 5, FIG.3; EX2036, Abstract, 3, 4. In the face of this evidence, PO offers no different or independent reason why claim 22 finds adequate written description support or an enabling disclosure where claim 21 fell short. PO’s argument with respect to the conserved nature of the two species of proteins (in addition to being incorrect and insufficient for predicting residual activity of the claimed proteins, for all of the

reasons Petitioner discussed in its Reply Brief (Paper No. 32, 11-20)), does not save claim 22 from being unpatentable.

C. Revised Claim 22 Violates § 42.121 Because it Adds New Matter.

As discussed, above, revised claim 22 covers the same unsupported scope as original claim 21 but instead introduces the idea that the claimed recombinant *Limulus polyphemus* Factor C proteins must be “higher than” Sf9-expressed *Limulus polyphemus* Factor C proteins or native *Limulus polyphemus* Factor C proteins. Paper No. 36, Appx. A. While PO characterizes the addition of the “higher than” limitations as “narrowing” (Paper No. 36, 3), such characterization is incorrect as discussed in Section II.A., *supra*. As such, these “higher than” limitations do not serve to limit claim 22 relative to original claim 21 at all. Of course, adding cosmetic detail to a claim where that detail merely overlaps with the existing limitations—as is the case here—does not narrow the claim (but rather exacerbates the § 112 deficiency).

In addition, the introduction of these “higher than” limitations introduces an entirely *different concept* into revised claim 22 relative to original claim 21—that the inventors somehow also possessed recombinant proteins from the *Limulus polyphemus* species of crab (whose underlying Factor C sequences had not yet been disclosed or elucidated) where such proteins would have residual activity values higher than *other Limulus polyphemus* Factor C proteins recombinantly

expressed in Sf9 cells or those natively sourced from the crabs themselves. The inventors undisputedly did not describe such proteins or the claimed comparisons between such proteins and so PO's addition of this relationship between *Limulus polyphemus* proteins constitutes an improper introduction of new matter.

III. REVISED CLAIM 22 IS STILL OBVIOUS OVER THE PRIOR ART OF THE INSTITUTED GROUNDS

PO's amended claim 22 would still have been obvious over the prior art at issue in the two instituted Grounds (1 and 2) of this trial.

A. Person of Ordinary Skill in the Art ("POSA")

As in its original Motion, PO again proposes an alternate definition of a POSA, attempting to discount Dr. Jain's qualifications. But as discussed in Petitioner's original Opposition, Dr. Jain has vast experience in this field. EX1003, ¶2; EX1065, 55:22-56:1, 57:6-8, 58:11-13, 59:2-4, 49:20-50:9, 50:12-19, 49:4-6, 63:14-20. He was unquestionably a POSA as of 2013. EX1069, 44:19-46:8; EX1067, 27:16-28:11; Paper No. 33, 7; EX1067, 33:7-11.

B. Revised Claim 22 Lacks An Adequate Written Description

1. As With Original Claim 21, the '767 Application Does Not Support The Reintroduced Functional Requirements of the Recombinant *L. Polyphemus* Factor C Proteins of Claim 22

As discussed above, revised claim 22 covers the same unsupported scope as original claim 21 and, fatally, PO makes the same insufficient argument for its patentability that this Board must have rejected as to claim 21 if it is now

considering claim 22. In particular, PO continues to argue that because the gross function of native Factor C in the coagulation cascade was thought to be overlapping between the four extant species of horseshoe crabs (i.e., within each species, Factor C was thought to function similarly in the presence of Factor B and Pro-clotting enzyme to detect endotoxin), such information would allow a POSA to make predictions about more specific (and as now claimed, relative) enzymatic activity (i.e., “residual activity”) of such proteins. Paper No. 36, 11-13. However, as Petitioner explained at length in its Reply, it was also known that the particular and specific enzymatic activity of Factor C (i.e., narrower measures of function in particular environments) exhibited significant variation across different assays, from which comparative conclusions between species could not be made. Reply, 11-20. Petitioner’s expert explained this in his Declaration (EX1002, ¶¶84, 91, 95-103) and PO’s experts conceded the existence of this uncertainty with respect to various studies of particular assays reporting complex differences in activity between different species of Factor C protein. EX1067, 154:12-156:13, 164:13-167:4, 161:18-162:18, 177:10-178:8, 178:1-21; EX1069, 58:7-59:6 (“The interference and interaction that occurs in such assays is multifactorial and very difficult to attribute to a...single origin.”).

PO cites *BASF Plant Sci., LP v. Commonwealth Sci. & Indus. Rsch. Organisation* in support of its argument for improperly gap-filling the ’767

Application with information that the '318 Patent inventors themselves unequivocally claimed as new and inventive three years *after* the alleged December 10, 2013 priority date and defended recently in Europe (EX1043, Reply, 4-6, n2), but *BASF* is plainly distinguishable—in multiple important respects—on its facts. 28 F.4th 1247 (Fed. Cir. 2022).

First, the specification at issue in *BASF* included significant discussion of the claimed plant species—canola—“includ[ing] numerous passages that expressly identify canola...as a preferred embodiment of the invention.” *Id.* at 1265. Here, other than noting that *Limulus polyphemus* was a known species of horseshoe crab, it is undisputed that the '767 Application never discusses *Limulus polyphemus* horseshoe crab Factor C or any Factor C sequence information from this species of horseshoe crab. EX1006, ¶¶3, 20, 46. Relatedly, the Court recognized in *BASF* that evidence of inventor skepticism with completing the invention in canola plants was of little weight because such inventor discussion occurred *before* success with the *Arabidopsis* plant—the plant that was more extensively described and exemplified in the specification—had been achieved. *BASF*, 28 F.4th at 1266. Here, the significant evidence of inventor skepticism relating to recombinant production of *Limulus polyphemus* Factor C proteins (and report of it having been achieved “for the first time in the world”) was dated three years *after* the alleged priority date in this case and well *after* recombinant production of Factor C

proteins in *Tachypleus tridentatus* had been reported. EX1005, ¶¶9-17, 25, 36, 46, 122, 180, 183; EX1073. **Most importantly**, the claims at issue in *BASF* **did not include** the specific levels of particularly-recited function that are at issue in this case with revised claim 22 (and original claim 21). In fact, the Federal Circuit pointed this out in *BASF* multiple times. *Id.* at 1265 (“The six Group A claims at issue here concern LC-PUFA production, **but none of them requires commercially desirable or other specific levels of such production.**”), 1267 (same).

Here, claim 22 **does** require specifically defined functional capabilities across a broad scope of residual activity values. But the ’767 Application does not describe the recombinantly produced *L. polyphemus* Factor C proteins across the full scope of (or any of the) residual activity values claimed. As such, *BASF* is not instructive in this case where PO is improperly trying to supplement its ’767 Application priority document—which actually points to a different and unclaimed horseshoe crab species as the “preferred embodiment” (EX1006, ¶20)—to support a claim to such unsequenced protein **with specific functional capability** across a broadly claimed range (and, per revised claim 22, to support a newly claimed relationship to other comparator proteins of the same unsequenced species).

On this last point, the Federal Circuit’s decision in *Centocor Ortho Biotech, Inc. v. Abbott Lab’ys*, is far more relevant. 636 F.3d 1341 (Fed. Cir. 2011). In *Centocor*, the Federal Circuit considered whether a claim to an isolated

recombinant anti-TNF- α antibody “with an affinity of at least 1×10^8 liter/mole”—which would include a fully human antibody with such functional property—was adequately described in a priority document that discussed a mouse antibody and a chimeric antibody with such property, but said “very little” about such an antibody with a human variable region. *Id.* at 1348-49. The functional requirement of the claims at issue in *Centocor* were central to that decision—as it is to the Board’s consideration here. And, while the sequence differences between the mouse and human variable regions of the antibodies claimed and described in *Centocor* were arguably greater than those between the various species of horseshoe crab Factor C proteins at issue in this case, the key points animating the Federal Circuit’s ruling are identical to the factual circumstances here. For example, in *Centocor*, as here, there was no evidence presented of anyone having made fully human antibodies to human TNF- α and the Court recognized that “[t]he fact that a fully-human antibody ***could be made*** does not suffice to show that the inventors of the [patent] possessed such an antibody.” *Id.* at 1350. Moreover, the Court noted that none of the evidence related to the “specific critical limitations in the asserted claims” (i.e., the functional requirements). *Id.* Likewise, here, there is no evidence measuring or comparing recombinant *Limulus polyphemus* Factor C proteins to any other species of protein on the claimed feature of residual activity across the broadly claimed range. Finally, the *Centocor* Court explained that the specification “does

not disclose any relevant identifying characteristics for such fully-human antibodies or even a single human variable region...[n]or does it disclose any ***relationship*** between the human TNF- α protein, the known mouse variable region that satisfies the critical claim limitations, and potential human variable regions ***that will satisfy the [functional] claim limitations.***” *Id.* at 1351. Likewise here, the ’767 Application provides no identifying characteristics of *Limulus polyphemus* Factor C proteins, nor any explanatory relationship between HEK293-recombinantly produced *Limulus polyphemus* Factor C and the claimed residual activity limitations. As the Court noted in *Centocor*, and is applicable here, “[t]he specification at best describes a plan for making fully-human antibodies and then identifying those that satisfy the claim limitations. But a ‘mere wish or plan’ for obtaining the claimed invention is not sufficient.” *Id.* at 1351.

2. Revised Claim 22’s Residual Activity “Higher Than” The Claimed Comparator Proteins Limitations Lack Written Description Support in the ’767 Application.

As with its first unsuccessful amended claim 22, PO’s newly revised amended claim 22 defines the scope of claimed recombinant *Limulus polyphemus* Factor C proteins, in part, by any that have a residual activity that is “higher” than either of two claimed comparator proteins (Sf9 expressed or native *Limulus polyphemus* Factor C proteins). But, as discussed in Petitioner’s Opposition to PO’s First Motion to Amend, this newly claimed relationship between the

recombinantly produced *Limulus polyphemus* Factor C proteins and the Sf9-expressed and native proteins is nowhere described in the '767 Application. PO points to the literal use of the phrase “higher residual activity” (relative to Sf9-expressed Factor C or native Factor C in the claimed ion solutions) in the specification in a laundry list of “modes” of the so-called “present invention” but nothing in the '767 Application describes an example of such a recombinant *Limulus polyphemus* Factor C protein with a residual activity relative to the claimed comparators (or describes any recombinant *Limulus polyphemus* Factor C protein at all). Nor does the '767 Application describe or surmise how or why the claimed recombinantly produced *Limulus polyphemus* Factor C proteins exhibit this relationship relative to Sf9-expressed or native proteins (or whether such is necessarily the case). These deficiencies parallel those of the claim at issue in *Novozymes A/S v. DuPont Nutrition Biosciences APS*, in which the Federal Circuit affirmed the invalidity for lack of written description of much-later filed claims to an alpha-amylase variant having “increased thermostability relative to the parent alpha-amylase.” 723 F.3d 1336 (Fed. Cir. 2013).

In *Novozymes*, the claim at issue was filed in 2009, claiming priority to its “original 2000 application,” and while the claim recited an “alpha-amylase variant” having “increased thermostability relative to the parent alpha-amylase,” the Federal Circuit recognized that the 2000 application “contains no disclosure of any

variant that actually satisfies the claims, nor is there anything to suggest that Novozymes actually possessed such a variant at the time of filing” the 2000 application. *Id.* at 1348. The Court likewise recognized that “[w]hile the 2000 application provides formal textual support for each individual limitation recited in the claims of the ’23 patent, it nowhere describes the actual functioning, thermostable alpha-amylase variants that those limitations together define.” *Id.* at 1349. Here, as in *Novozyms*, PO points to the textual words of the features of claim 22, but cannot point to disclosure of any functioning Factor C protein that the claims actually cover. Moreover, the *Novozyms* Court recognized that while Novozymes had provided examples showing that it tested and verified “some [unclaimed] thermostable variants,” “nothing in the 2000 application demonstrates that it had verified whether any of the [claimed position substitutions] actually yielded a thermostable variant.” *Id.* As is true here, the Court in *Novozyms* aptly noted that “if Novozymes had possessed a working variant” as claimed, “it surely would have disclosed that[.]” *Id.*

In the instant case, as in *Novozyms*, PO ***hypothesizes*** that a recombinantly produced *Limulus polyphemus* Factor C protein will exhibit the claimed “higher residual activity” relationship relative to Sf9-expressed and native protein based on the fact that the specification provides a single example of such protein for a different, unclaimed, species of Factor C protein. But the ’767 Application

provides no verification of this hypothesis, nor does it provide any guidance that the inventors were in possession of the vast array of degrees of “higher” residual activity relationships that revised claim 22 conveys (i.e., slightly higher, moderately higher, vastly higher, etc.). Nor does the ’767 Application provide any explanation as to whether the claimed recombinant *Limulus polyphemus* Factor C protein will always exhibit a residual activity higher than the comparator proteins (for example, because of a structural feature) or whether the inventors were merely claiming scenarios in which this ***happened*** to be the case.

As discussed in the Petition, the ’767 Application speculates that the addition of post-translation (α -2,3)-linked terminal sialic acid via expression in mammalian systems (such as HEK293 cells) ***could*** contribute to such increase in residual activity. Pet. 36-37. But the ’767 Application provides no description of a mammalian-expressed *Limulus polyphemus* Factor C protein exhibiting a “higher” residual activity than the comparator proteins, nor does the ’767 Application provide any explanation by the inventors for how this could be achieved.

Confirming their lack of understanding as to the relationship between residual activity and mammalian-expressed recombinant Factor C proteins versus non-mammalian expressed (or native) proteins, the inventors later abandoned the “sialic acid” theory for why Factor C proteins expressed in mammalian cells (whose post-translational modifications included the addition of an (α -2,3)-linked

terminal sialic acid) exhibited higher residual activities than in proteins where such post-translational modification does not occur (i.e., in insect (Sf9)-expressed and native proteins). EX1004, 77 (“[S]uperior salt tolerance can be reproduced irrespective of presence of (α -2,3)-linked terminal sialic acid, at least for *Limulus* Factor C recombinantly produced using HEK 293 cell as a host.”), 86 (same); EX1002 (Jain), ¶107. Just as the undescribed but claimed variant in *Novozymes* lacked written description support because “prediction” about the claimed increased thermostability did not amount to “possession,” so too does revised claim 22 lack written description support here. *Id.* at 1350.

C. Revised Claim 22’s Recitation of Recombinant *Limulus polyphemus* Factor C Proteins With Residual Activities “Higher Than” The Claimed Comparator Proteins Is Not Enabled

Revised claim 22 adds the non-limiting feature of a relative (“higher”) relationship between the residual activities of the claimed recombinant *Limulus polyphemus* Factor C proteins and two comparator proteins (Sf9-expressed and native *Limulus polyphemus* Factor C proteins). Revised claim 22 (like claim 21) remains open-ended and covers HEK293 recombinantly produced *Limulus polyphemus* Factor C proteins with residual activities as low as 10% in the presence of 21 mM sodium citrate or 15% in the presence of 16 mM magnesium sulfate, or as high as any unbounded upper value that still surpasses the Sf9-expressed or native values. And yet, as with claim 21, none of the ’767

Application, PO, nor its experts, has any explanation for a POSA about how to make and use such proteins at the lower, middle, or highest points of this range, nor is there any explanation for how to make and use such proteins falling with the range as distinct from those falling outside of it. The task of figuring that out is instead left to the POSA to accomplish through significant experimentation.

EX1002, ¶¶119-146. Dr. Jain detailed at length why the '767 Application's deficiency in this regard would have required the POSA to have engaged in significant and undue experimentation to answer these questions as to claim 21, which would also be applicable to claim 22, which is of the same non-enabled scope. EX1002, ¶¶105-108, 119-126, 131-138, 140-146.

In its Preliminary Guidance, this Board found Petitioner's cited cases—*MagSil Corp. v. Hitachi Glob. Storage Inc.*, 687 F.3d 1377, 1383-84 (Fed. Cir. 2012) (no enablement of claims to “a change in the resistance by at least 10%” because the specification only enabled changes in resistance up to about 12% yet the claims claimed resistance changes up to infinity) and *Epistar Corp. v. Lowes Cos., Inc.*, No. LA CV17-03219, 2020 WL 771096, at *6-8 (C.D. Cal. Feb. 11, 2020) (no enablement for claim reciting “wherein the light-emitting structure has a light output power of more than 4 mW at 20mA current”)—inapposite because they related to *particular levels of a property* whereas originally proposed claim 22 simply required the claimed recombinant proteins to have a “higher residual

activity” than the comparator proteins. Paper No. 34, 13-14. However, now that PO has imported such “levels” **back into** revised claim 22 with its negative exclusionary limitations, *MagSil* and *Epistar* are once again directly on point and demonstrate why revised claim 22 lacks an enabling disclosure. As discussed in the Petition, the ’767 Application does not teach a POSA to make and use the functionally claimed recombinant *Limulus polyphemus* Factor C proteins at the levels claimed (i.e., from 10% or 15% up to 100% or greater) without undue experimentation. Pet., 36-42; EX1002, ¶¶130-146.

In addition, contrary to PO’s assertion, and having amended claim 22 to again recite the numerical levels of claim 21, *Alcon Rsch. Ltd. v. Barr Lab’ys, Inc.* is not on point. The claim at issue in *Alcon* was a method claim for “enhancing the chemical stability of an aqueous composition.” 745 F.3d 1180, 1184 (Fed. Cir. 2014). The Court determined that such claimed method “comprise[s] only a single step—adding a chemically-stabilizing amount of PECO to the prostaglandin composition—that [the challenger’s] own expert testified was ‘routine.’” *Id.* at 1189. The Court noted that the specification at issue disclosed “exemplary compositions within the scope of the claims, detail[ed] how those example compositions are prepared from commercially-available ingredients, and provide[d] step-by-step procedures for adding PECO to a prostaglandin composition in a way that embodies the claimed invention.” *Id.* As such, the

Court found that the challenger did not even make a “threshold showing that *any* experimentation is necessary to practice the claim methods” let alone undue experimentation. *Id.* These facts and analysis are inapplicable to revised challenged claim 22, which (like claim 21) claims recombinant *proteins* of a species of horseshoe crab whose underlying gene and amino acid sequences were *not disclosed* in the ’767 Application and had not yet been elucidated or reported anywhere in the art as of the filing of the ’767 Application, and which claims such proteins having a particular functional capability defined broadly to encompass any such proteins having a residual activity of 10% (or 15%) or higher in certain ionic concentrations. As Dr. Jain testified both in his declaration and under cross-examination, practice of the full scope of claim 21 (and by extension revised claim 22) would have required a POSA to engage in undue experimentation. EX1002, ¶¶130-146, EX1065, 96:1-98:13. In view of this testimony, the ’767 Application fails to enable the full scope of revised claim 22.

D. Revised Claim 22 is Obvious Over the Prior Art

PO again argues that Petitioner’s “reasonable expectation of success theory cannot be squared with its assertions relating to the lack of Section 112 support” (Paper No. 36, 20-21) but refuses to acknowledge the different legal standards between §§ 112 and 103 and ignores that applicant was required to describe and enable *the full scope* of its broadly and functionally claimed Factor C proteins.

For all of the reasons discussed in Sections II and III, *supra*, the Petition, Section IX.B., and the Reply, Sections II-V., by December 10, 2013 the full scope of claim 21 was neither described nor enabled. As Dr. Jain testified, however, by April 30, 2019, a POSA reading Mizumura's reports on residual activity in *Tachypleus tridentatus* Factor C and having access to the then-published sequence information for *Limulus polyphemus* Factor C and the experimental results of the '498 PCT would have found it obvious to try to generate an example of a HEK293-recombinantly produced *Limulus polyphemus* Factor C protein and would have reasonably expected that protein to fall within the claimed residual activity range, and higher than the comparators. EX1002, ¶¶156-192; EX1065, 130:9-131:21.

Because the enablement and written description requirements look *to the full scope of the challenged claim*, the prior art can render an embodiment that falls within the scope of the claim obvious, while that prior art (viewed with the teachings of the patent) do not enable or describe the full scope of the claim. There is no inconsistency. *Parus Holdings, Inc. v. Google LLC*, 70 F.4th 1365, 1374 (Fed. Cir. 2023) (precedential); *In re Mraz*, 455 F.2d 1069, 1072-73 (CCPA 1972); *Pharm. Res., Inc. v. Roxane Lab'ys, Inc.*, No. 03-3357, 2006 WL 3231427, at *16 (D.N.J. Nov. 8, 2006). Moreover, this Board has recognized that the "reasonable expectation of success" inquiry and those involving 35 U.S.C. § 112 are *different*. *Arkema Inc. v. Honeywell Int'l Inc.*, PGR2016-00012, 2016 WL 5404194

(P.T.A.B. Sept. 2, 2016) (granting institution—“A reasonable expectation of success of achieving one composition within the scope of the claim, however, differs from reasonably enabling the full scope of the claim.”).

PO makes no other argument regarding why claim 22 would not be obvious over the prior art should this Board determine that it is not entitled to the December 10, 2013 priority date.⁴ Thus, if claim 22 is found to lack written description support or an enabling disclosure from the '767 Application, that claim (like claim 21) should be entitled to a priority date of no earlier than April 30, 2019 and prior art references Mizumura in combination with either the '498 PCT or McClymont would have rendered claim 22 obvious to a POSA.

IV. CONCLUSION

For the foregoing reasons, entry of revised claim 22 should be denied.

Respectfully submitted,
Charles River Laboratories, Inc.

Date: May 6, 2026

/Chelsea A. Loughran/
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⁴ PO says nothing in its Revised Motion regarding unexpected results. Should PO raise such evidence in Reply, Petitioner has already rebutted it. *See* Reply, 24-26.

CERTIFICATE OF SERVICE UNDER 37 C.F.R. § 42.6 (e)(4)

I certify that on May 6, 2026, a copy of the foregoing document, including any exhibits filed therewith, is being served via electronic mail, as previously consented to by Patent Owner, upon the following:

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