

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

**PETITIONER’S OPPOSITION TO PATENT OWNER’S MOTION FOR
ADDITIONAL DISCOVERY UNDER 37 C.F.R. § 42.51(b)(2)(i)¹**

¹ Sections I-III of this Opposition provide specific responses to PO’s characterizations of inconsistency and evidence refuting the same and so are different than the corresponding sections in the Opposition in IPR2025-00440. Section IV in both briefs are nearly identical.

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LISTING OF EXHIBITS

Exhibit	Description
1001	U.S. Patent No. 11,959,109
1002	Prosecution History of U.S. Patent No. 11,959,109 (Application No. 18/346,420)
1003	Declaration of Siddhartha Jain, Ph.D., PMP (“Jain”)
1004	Curriculum Vitae of Dr. Siddhartha Jain, Ph.D., PMP
1005	International Patent Publication No. WO 2018/074498 A1
1006	Higdon et al., “Modeling sequence and function similarity between proteins for protein functional annotation,” <i>Proc Int Symp High Perform Distrib Comput.</i> 2010: 499–502.
1007	Kobayashi et al., “Factor B Is the Second Lipopolysaccharide-binding Protease Zymogen in the Horseshoe Crab Coagulation Cascade,” <i>J Biol Chem.</i> 2015 Jun 24; 290(31):19379–19386.
1008	Japanese Priority Application No. JP2012-269840 (certified translation)
1009	U.S. Patent No. 5,716,834
1010	Muta et al., “Limulus Factor C. An endotoxin-sensitive serine protease zymogen with a mosaic structure of complement-like, epidermal growth factor-like, and lectin-like domains,” <i>J Biol Chem.</i> 1991 Apr 5; 266(10):6554-61.
1011	Karen McClymont, Ph.D. Thesis, submitted in fulfilment of the requirements for the Degree of Doctor of Philosophy from the University of Glasgow, Institute of Molecular, Cell and Systems Biology College of Medical, Veterinary and Life Sciences, March, 2017
1012	U.S. Patent Application Publication No. 2021/0363564
1013	Declaration of Dr. Mary K. Bolin
1014	RESERVED
1015	U.S. Patent Application Publication No. 2019/0241629
1016	U.S. Patent Application Publication No. 2015/0307864
1017	U.S. Patent Application No. 14/650,767, as filed June 9, 2015
1018	RESERVED
1019	Shi et al., “Protein N-Glycosylation in the Baculovirus-Insect Cell System,” <i>Curr Drug Targets.</i> 2007 Oct; 8(10): 1116–1125.
1020	RESERVED
1021	RESERVED
1022	Transition Certification for U.S. Patent Application No. 15/983,725, filed May 31, 2019.
1023	RESERVED

1024	RESERVED
1025	Tokunaga, F., et al. "Further studies on lipopolysaccharide-sensitive serine protease zymogen (Factor C): Its isolation from <i>Limulus polyphemus</i> hemocytes and identification as an intracellular zymogen activated by α -chymotrypsin, not by trypsin," <i>J. Biochem.</i> 1991 Jan; 109(1):150-7.
1026	Dwarakanath, R.S. et al., "Recombinant COS-1 cells express <i>Carcinoscorpius rotundicauda</i> Factor C," <i>Biotechnology Letters</i> . 1997 April; 19(4):357-61.
1027	Wang, J. et al., "Functional expression of full length <i>Limulus</i> Factor C in stably transformed Sf9 cells," <i>Biotechnology Letters</i> . 2001; 23:71-76.
1028	RESERVED
1029	RESERVED
1030	Barrabes, S. et al., "Effect of sialic acid content on glycoprotein p/ analyzed by two-dimensional electrophoresis," <i>Electrophoresis</i> . 2010 Sep; 31(17):2903-12.
1031	Palomares, L.A., "Production of Recombinant Proteins: Challenges and Solutions," From: <i>Methods in Molecular Biology</i> , vol. 267: Recombinant Gene Expression: Reviews and Protocols, Second Edition Edited by: P. Balbás and A. Lorence © 2004 Humana Press Inc., Totowa, NJ, pp. 15-51.
1032	RESERVED
1033	RESERVED
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1036	RESERVED
1037	RESERVED
1038	Sekiguchi, K. and Shuster, C.N., "Limits on the Global Distribution of Horseshoe Crabs (Limulacea): Lessons Learned from Two Lifetimes of Observations: Asia and America," <i>Biology and Conservation of Horseshoe Crabs</i> , 2009.
1039	Hossler et al., "Optimal and consistent protein glycosylation in mammalian cell culture," <i>Glycobiology</i> . 2009 Sep; 19(9):936-4.
1040	File History of United States Application No. 16/399,386
1041	ExpiCHO™ Expression System - USER GUIDE – For transfection of ExpiCHO-S™ in a defined, serum-free medium. Catalog Number A29133, Publication Number MAN0014337 Revision D.0 (May 25, 2018).

1042	U.S. Appln. No.: 17/554,128, “Novel Recombinant Factor C And Method for Producing the Same, and Method for Measuring Endotoxin” Non-Final Office Action, Mar. 20, 2025 (“128 App. NFR”)
1043	European Patent No. 3530670, “Method for producing endotoxin detecting agent comprising recombinant limulus factor c and use thereof,” Response to Opposition, May 9, 2025
1044	European Patent No. 3441466, “Method for Producing a Novel Recombinant Factor C, Method for Mitigating Reaction Inhibition In Endotoxin Assays, And Method for Measuring Endotoxin,” Decision on Opposition, Oct. 26, 2022
1045	USP, General Chapter Prospectus: Use of Recombinant Reagents in Bacterial Endotoxins Test. May 29, 2020
1046	Stewart, C.M., “Interim Processes for PTAB Workload Management,” Memorandum dated March 26, 2025
1047	U.S. Appln. No.: 17/554,128, “Novel Recombinant Factor C And Method for Producing the Same, and Method for Measuring Endotoxin” Amendment under 37 C.F.R. § 1.111, Jan. 28, 2025
1048	European Patent No. 3530670, “Method for producing endotoxin detecting agent comprising recombinant limulus factor c and use thereof,” Notice of Opposition, Nov. 22, 2024
1049	RESERVED
1050	U.S. Appln. No.: 16/331,810, “Recombinant Proteins Derived From Genus Limulus, and DNA Molecules Encoding Same,” Notice of Abandonment, Mar. 14, 2023
1051	Press Release, “USP Provides Guidance on the Use of Recombinant Reagents for the Bacterial Endotoxin Test.” May 29, 2020
1052	RESERVED
1053	U.S. Appln. No.: 14/650,767, “Novel Recombination Factor C and Method for Producing the Same, and Method for Measuring Endotoxin,” Non-Final Office Action, Sept. 16, 2016
1054	RESERVED
1055	RESERVED
1056	U.S. Appln. No.: 18/346,420, “Novel Recombinant Factor C and Method for Producing the Same, and Method for Measuring Endotoxin,” Non-Final Office Action, Sept. 15, 2023
1057	R. Davis, Acting USPTO Leader Says New Policies Will Bolster Patents, Law360 (Apr. 1, 2025), https://www.law360.com/articles/2316863/ (accessed June 10, 2025)

1058	U.S. Appln. No.: 14/650,767, “Novel Recombination Factor C and Method for Producing the Same, and Method for Measuring Endotoxin,” Preliminary Amendment, Jun. 9, 2015
1059	U.S. Patent No. 10,144,923
1060	U.S. Patent No. 10,982,202
1061	U.S. Patent No. 6,391,570
1062	Transcript of August 1, 2025 Conference Call
1063	Email from McKeown, Scott, RE: PGR2025-00023 and IPR2025-00440: Request for Position on Motions to Compel Routine Discovery (Jun. 25, 2025)
1064	Declaration of Chelsea A. Loughran in Support of Admission <i>Pro Hac Vice</i>
1065	Transcript of November 4, 2025 Deposition of Siddhartha Jain, Ph.D., PMP

I. INTRODUCTION

PO bases its request for additional discovery (Mot.)—just as it did its request for routine discovery—on excerpted statements in an EP Opposition (EPO) challenging the inventive step of sequencing and recombinantly producing *L. polyphemus* Factor C proteins as of Oct. 18, 2016. Studiously avoiding any discussion of necessary context or the fact that Petitioner here challenges the sufficiency of written description and enablement of the full scope of a far broader claim to recombinant horseshoe crab proteins, configured in thousands of combinations, as a working assay for endotoxin detection, PO concludes there is an “inconsistency” between proceedings. But the panel already told PO: “*the claims...at issue in the Opposition are different and both broader and narrower than the challenged claim in this proceeding in different respects. Neither has [PO] explained why the grounds on which the Opposition is based are necessarily inconsistent with positions advanced by Petitioner in this proceeding.*” Paper 17, 4-5 (internal citations omitted).

PO’s withholding of necessary context and available information continues here. A week prior to filing its Motion, PO deposed Petitioner’s declarant, Dr. Siddhartha Jain, which PO conspicuously says nothing at all about. Dr. Jain unequivocally explained why—in his scientific opinion—there is no inconsistency between the Declaration of Dr. Frohman (filed in the EPO) and the arguments of

Petitioner in this PGR. He testified that he viewed Dr. Frohman's testimony in proper scientific context to be consistent with his own before this Board:

Q Paragraph 107 in Exhibit 2, your PGR declaration. So in this paragraph, you state that, "In my experience and in the experience of a POSA in the field of recombinant protein production, the translatability of expression process across proteins cannot be assumed." Do you see that?

A Yes.

Q And that is your opinion, correct?

A That is what I just stated as well earlier.

Q And you don't view that as inconsistent with Professor Frohman's opinions that we were just looking at [EX2004 (Frohman Decl., ¶47)]?

A Yes, I don't see that as being inconsistent. Specifically this paragraph talks about the assertion that the inventors made of using the same procedure that was used for Factor C to express Factor B and proclotting enzyme, which are quite different proteins. And like I mentioned, that when we are -- what Dr. Frohman is talking about is not expressing Factor B or proclotting enzyme. All he's talking about is yes, the inventors were able to express Tachypleus Factor C using Sf9, CHO and HEK cells. Therefore, *Limulus* Factor C could also be expressed. And we are generally aligned because I've said that I believe a POSA would have a reasonable expectation.

EX1065 (Jain Depo.), 81:12-82:23, *see also, id.*, 86:18-87:20, 185:12-186:15. Dr.

Jain's analysis as to lack of possession of (and amount of experimentation required

to generate) the thousands of combinations of proteins capable of detecting endotoxin across the full scope of claims 1-9 in 2013 is not inconsistent with the fact that obtaining an exemplary Factor C protein would have been reasonably expected by a POSA several years later. *Id.*, 81:12-82:18.

Even setting aside PO's withholding of necessary scientific context and week-old testimony directly on point, PO has not explained why the discovery it seeks is *relevant* to its claimed invention, which lacks written description and enablement, as of 2013. That is, even accepting PO's ostensible argument that somehow the EPO acknowledges a possible later priority date for the claim at issue there (which is hypothetical since the EPO is only considering the question of inventive step (*obviousness*) of a recombinant *L. polyphemus* Factor C protein as of 2016), PO has made clear in its own words— it *is not arguing for such an intervening date in this PGR*. EX1062, 25:6-14.

PO's Motion abuses the additional discovery mechanism for the sole purpose of injecting conspiratorial distraction into the record and should be denied.

II. PO HAS FAILED TO SHOW THE RELEVANCE OF THE REQUESTED DISCOVERY

PO's request for additional discovery does not demonstrate how the requested information—confirming whether Petitioner initiated the EPO—is relevant to this PGR. PO has pointed to no affirmative evidence supporting such relevance, and has ignored new evidence explaining why no inconsistency exists.

A. Dr. Jain Explained Why There Is No Inconsistency

With respect to the question of inconsistency, PO claims that “[i]t is immaterial that the claims involved in the Opposition are different than those at issue here.” Mot. 4. But Dr. Jain explained why this difference in scope accounts for the difference in opinions and arguments advanced in the EPO and before this Board. In particular he explained why Dr. Frohman’s explanation of using RACE techniques to generate cDNA for the *L. polyphemus* Factor C sequence does not account for the complexity of generating and forming an assay out of all the proteins required by the full scope of the claims 1-9 of the ’109 Patent:

So when we look at Dr. Frohman's declaration, we have to understand that it's not just about the use or not use of RACE technology, because that's -- that's somewhat of an opinion focused only on the sequencing of mRNA. *There are other elements that are involved in sequencing the Factor C, Factor B and Tachy -- and proclotting enzyme mRNA. And the complexities might have been related to other challenges, not just related to what specific sequencing methodology was used.* So, for example, when you look at the '498 PCT or '629 specification, the inventors noticed that one of the PCR products did not actually show in the gel....Now, it could be because the PCR had an issue, but it could also mean that the quality and quantity of mRNA that was obtained from *Limulus* -- *Limulus* blood was of not the same degree as the Tachypleus, and that could relate to the differences in diversity that the inventors talk about. There are also other challenges like -- that we already see in '419 PCT, existence of

variance due to polymorphism, and also it was known that because a whole genome duplication in *Limulus*, there were instances of paralogs. So being able to identify those variants could have added to the complexity....But it's clear from their procedure that from -- there was some differences, some challenges that they faced with regards to getting amplification -- DNA amplification.

EX1065, 171:10-173:6. Dr. Jain's accounting for such challenges as they relate to the other proteins encompassed by claims 1-9 explains, in part, why Dr. Frohman's opinions regarding the obviousness of sequencing and expressing *L. polyphemus* Factor C are not inconsistent with Dr. Jain's testimony regarding the experimentation required to overcome the challenges with describing and making and using the full scope of functional proteins encompassed by the challenged claims. *See Arkema Inc. v. Honeywell Int'l Inc.*, PGR2016-00012, Paper 13, at 35 (P.T.A.B. Sept. 2, 2016) (granting institution—"[PO] contends that Petitioner has presented inconsistent arguments concerning enablement as Petitioner has stated that [a POSA] had a reasonable expectation of success of achieving the limitation of claim 13....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."); *Liquidia Techs., Inc. v. United Therapeutics*, IPR2021-00406, Paper 78, at 32-33 (P.T.A.B. July 19, 2022) ("Reasonable expectation of success is a separate inquiry from enablement....[T]hat [the expert] testifies to a

lack of enablement in one forum and to the presence of a reasonable expectation of success in a second forum does not render unreliable the testimony in either.”).

B. PO Saddles Petitioner With The Inventors’ Inconsistencies

Any inconsistency in this proceeding flows from the *inventors’ own statements*. PO points to the ’498 PCT and purportedly inconsistent “characterizations” of that reference. Mot. 2. That the inventors made these admissions is a fact, and their significance has different relevance to different legal questions at different points in time. In the ’498 PCT, the inventors of claims 1-9 stated that “*it has not been possible* to accurately determine the full-length sequence structure, expression, and function of [*L. polyphemus* zymogen] proteins and genes using conventional methods.” EX1005, ¶12 (emphasis added). In the context of whether such inventors described and enabled the full scope of broad claims to thousands of combinations of recombinantly produced zymogen proteins in an assay, including but extending far beyond recombinantly produced *L. polyphemus* Factor C proteins, the inventors’ statements that this protein had *not* been identified “structurally and functionally” (*id.*, ¶10) is highly relevant. Such statements may be less relevant to the question of whether such proteins were obvious several years later. In any case, this Board can assess and weigh the fact of the inventors’ statements.

Finally, PO reduces the question of undue experimentation of the challenged claims to the sequencing *L. polyphemus* Factor C by 2016. Mot. 3. But that reduction ignores the full scope of the challenged claims beyond one protein, fails to account for the challenges associated with generating sequences for all claimed proteins in order to produce them recombinantly (as Dr. Jain testified to: EX1065, 171:10-173:6), and confirms that even if the generation of *L. polyphemus* Factor C were obvious at some later date, the inventors were not in possession of (nor had enabled) the full scope of the claimed assay agent in 2013, particularly where they did not describe a single example within such scope (even for constituent proteins whose sequences were known). EX1065, 147:21-148:13; 131:22-132:20.

The inventors admitted to a struggle in sequencing *L. polyphemus* Factor C well after 2013. Mot. 4 (citing Pet., 42, which cites the '498 PCT). That such statements are highlighted in this PGR does not show inconsistency on the part of Petitioner. If anything, the veracity of PO—now claiming to have invented, by 2013, recombinant proteins including *L. polyphemus* Factor C but also thousands of combinations of zymogen proteins as a functional assay—should be questioned.

III. PO HAS NOT DEMONSTRATED THAT THE REQUESTED DISCOVERY IS IN THE INTEREST OF JUSTICE.

A. *Garmin* Factor 1

Factor 1 supports denial as the alleged inconsistency is already in the record via EPO filings, and, as discussed in Sections I and II, *supra*, the arguments in the

EPO are *not* inconsistent with Petitioner’s arguments in this PGR. Petitioner’s expert explained in detail at his deposition how the various statements and arguments cited in the Board’s order (Paper 17, 7-8) are scientifically consistent. *See* §§ I-II, *supra*. PO has not explained why its requested “confirmation” is useful to any disputed issue in the PGR. The Board is fully capable of weighing the facts and relevant expert testimony on the science.

B. *Garmin* Factor 2

The EPO affords an Opponent anonymity for several reasons including that he should not be “obliged to reveal to the patent proprietor why a patent disturbs him.” G 0004/97, 15-17 (Jan. 21, 1999). PO’s cursory statement that the requested information does not seek Petitioner’s litigation positions (Mot. 5) is incorrect as revelation of the identity of an anonymous EP Opponent is tantamount to revealing litigation strategy. *See* § III, *infra*. PO cites no authority to the contrary.

C. *Garmin* Factor 3

PO argues: “PO cannot generate the information without the requested discovery.” Mot. 5. This is untrue. PO wants this Board to associate the EPO with Petitioner, which the Board may or may not do without forcing Petitioner to waive its privileges. The requested discovery is unnecessary.

D. *Garmin* Factor 4

PO did not attach any formal discovery request or define any terms, so as to render its discovery request “easily understandable.”

E. *Garmin* Factor 5

PO says it is seeking a “simple answer.” Mot. 5. However, PO is asking Petitioner to reveal its attorney-client privileged and work product legal strategy and such forced revelation could be leveraged to argue for a broader waiver.

IV. PO CANNOT COMPEL A WAIVER OF ATTORNEY-CLIENT PRIVILEGE OR ATTORNEY WORK PRODUCT IMMUNITY.

PO copies its privilege argument (Mot., 6-10) almost verbatim from its prior failed motion (Paper 12, 3-7) without addressing Petitioner’s prior Opposition. Paper 13, 6-7. Again, PO cites zero authority permitting the Board to compel a party to confirm/deny anonymity (and attorney-client privilege and work product immunity arising from its EPO litigation strategy. While there is no question that Charles River is the client of Wolf Greenfield, any disclosure by Petitioner or Wolf Greenfield confirming or denying involvement (Petitioner’s or any other entity’s) in the anonymous EPO (*i.e.*, legal strategy and whether to employ the same in a confidential proceeding) in a very small competitive space, would reveal confidential attorney-client communications and further risk waiver of the same.

Moreover, work-product immunity covers documents and communications created in anticipation of post-issuance patent challenges. Fed. R. Civ. P. 26(b)(3); *see Applied Telematics, Inc. v. Sprint Commc’ns. Co., L.P.*, 1996 WL 539595, *3-6 (E.D. Pa. Sept. 18, 1996). And in the analogous context of anonymous *ex parte* reexaminations, multiple Courts have ***declined*** to compel the identification of a

requesting party where, as here, such identity is only “marginally relevant” and so “protecting the confidentiality of the requester outweighs [POs] interest in discovery the identity of the requester.” *Davco Mfg. Corp. v. Peninsular Diesel, Inc.*, 128 F.R.D. 91, 92 (N.D. Ohio 1989); *TQ Delta, LLC v. DISH Network Corp.*, No. 1:15-cv-00614-GBW, ECF No. 407, at 6-8 (D. Del. Mar. 1, 2022) (declining to compel discovery relating to *ex parte* reexam where movant failed to show relevance of EPR positions and any interest in the discovery was “outweighed by...safeguards imposed to ensure confidentiality of the requester’s identity”).

Petitioner has more than met its burden to show that the requested discovery, ***which has no useful relevance to the PGR grounds at issue here***, does not outweigh the significant confidentiality interests protecting Petitioner’s work product developed in anticipation of litigation. Any inconsistency between this PGR and the EPO arises from ***the inventors’ own duplicitous strategy*** of claiming to have invented a broad scope of functional zymogen proteins including those from *L. polyphemus* as of 2013, while telling the world several years later — to secure an additional patent — that ***only then*** had they finally “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.” EX1005, ¶17. PO’s request for additional discovery should be denied.

Date: November 21, 2025

Respectfully submitted,

/Scott A. McKeown/

Scott A. McKeown, Reg. No. 42,866

WOLF, GREENFIELD & SACKS, P.C

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

I certify that on November 21, 2025, 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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