UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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CHARLES RIVER LABORATORIES, INC.,
Petitioner,

v.

SEIKAGAKU CORPORATION,
Patent Owner.

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

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PETITIONER'S RESPONSIVE SUPPLEMENTAL BRIEF

Teva Pharms. Int'l GmBH v. Eli Lilly & Co. ("*Teva*") applied preexisting Federal Circuit precedent to claims "pertain[ing] to a well-known genus that is not, itself, the invention." Moreover, the specification in *Teva* disclosed a working example of the pre-existing genus and indicated that ***all*** members of such genus accomplished the claimed method. The disputed claims here are fundamentally different. By PO's own account, the '318 Patent invention concerned a new genus of recombinant proteins with unpredictable activity levels. And the '109 Patent claims a method of generating a new genus of endotoxin assay agents comprising combinations of functional, mammalian-expressed, recombinant proteins where the secretion of Factor C as claimed likewise generated "unexpected" levels of Factor C activity. Yet in both cases, the specification fails to disclose a single species satisfying the claimed functions. *Teva* does not inform the outcome of this dispute.

I. IPR2025-00440

The *Teva* court cautioned that claims drawn to a "novel" genus would involve a "different question." *Teva*, 12. And this Board does face a different question because claim 21 recites an allegedly novel genus of recombinant *L. polyphemus* Factor C proteins having a claimed residual activity. In view of these and the distinctions discussed below, *Teva*'s analysis dictates the opposite answer.

Not a well-known genus: Claim 21 encompasses a broad genus of Factor C proteins across a claimed range of possible residual activity percentages. It is

undisputed that the claimed recombinant *L. polyphemus* proteins had not been made and the underlying gene and amino acid sequences had not been elucidated or reported by December 10, 2013. EX1006, EX2038, ¶35. "Residual activity" was not a routinely measured metric, but instead, per applicant, revealed "unexpected" values fueling applicant's arguments for patentability. EX1004, 75-78, 82-87, 149-153, 175-179. Unlike in *Teva,* the '318 Patent specification is clear that the genus of recombinant proteins with such residual activity ***is the invention***: "The present inventors have found that a recombinant horseshoe crab Factor C can be produced by use of human cells …while reaction inhibition in the presence of a salt (ion) is mitigated." EX1001, 3:12-19. Claim 21 does not recite a well-known genus.

No link between genus and function: It was undisputed and core to the *Teva* decision—mentioned five times in the opinion—that a reasonable jury could have found that ***all humanized anti-CGRP antagonist antibodies treat headache***. *E.g., Teva*, 5, 13. By contrast, here, there is no evidence from which the factfinder could conclude that ***all*** recombinant *L. polyphemus* Factor C proteins will have the residual activity claimed. Instead, long after the claimed priority date, the inventors abandoned the one structural limitation thought to drive such function and negated it as an explanation for their observation of residual activity. EX1004, 85-86.

No species/example disclosed: The specification at issue in *Teva* indisputably disclosed a working example of the humanized anti-CGRP antagonist

antibody used for the claimed method. By contrast, the '767 Application priority document indisputably fails to disclose ***any*** examples of the claimed genus of recombinant *L. polyphemus* proteins. Nor does it disclose any structural feature common to such genus of proteins ***with*** the claimed residual activity. These omissions are dipositive under *Ariad* for purposes of written description.

Not "routine" to complete the genus: It was undisputed in *Teva* that a reasonable jury could have found that the process of humanizing antibodies was routine. In view of this, the Court found that a POSA could have combined such routine procedures ***with*** the single disclosed example ***and*** the fact that all humanized anti-CGRP antagonist antibodies treat headache to envision the complete genus. *Teva*, Slip Op. 13-14. None of this is true here. In this IPR, the inventors themselves disclosed (three years ***after*** the alleged priority date), that obtaining the coding sequences for *Limulus polyphemus* Factor C and recombinantly producing them was anything but routine—and had been accomplished "for the first time" in 2016. EX1005, ¶¶01-17, 25, 36, 46, 67-68, 122, 180, 183. Separately, the inventors secured claim 21 based on their insistence during prosecution that the residual activity values of the later-sequenced *L. polyphemus* Factor C proteins were unexpected (though PO's evidence of the same here is insufficient). *See e.g.,* EX1004, 75-78; Reply, 24-26. Moreover claim 21 requires ***specific*** residual activity values defined by the recited open-ended ranges,

whereas the claims in *Teva* were flexible—any "effective amount" was sufficient. Here, unlike in *Teva,* the inventors left POSAs to complete their invention.

II. PGR2025-00023

Not a well-known genus: Challenged claims 1-9 broadly require ***making*** an endotoxin detection assay via the recombinant expression of ***functional*** Factors C, B, and Pro-clotting enzyme, from any of several recited species of horseshoe crab, using any of several mammalian expression systems, in any mix-and-match grouping. EX1001, cls. 1-9; EX1003, ¶¶55-58. Despite PO's assertion that the proteins comprising this endotoxin detection assay were "well-known and widely available" (Supp. Br. 3), PO cites evidence relating to the ***native*** proteins and the underlying bulk sequence information for one possible species of horseshoe crab recited as part of the larger claimed genus. PO points to no prior art disclosure of the making of such grouping of functional proteins (Factors B, C, and Pro-clotting enzyme) expressed in mammalian cells as endotoxin detection assays, because this is the alleged invention itself. In contrast to *Teva* (where the claims were directed to administering antibodies—not making them), the methods of challenged claims 1-9 are not a "well-known genus used as part of a different invention".

No link between genus and function: The evidence of record demonstrates that a POSA would ***not*** expect that all of the mammalian expressed proteins from claim 1 will have their intended "activity" and work as the claimed "endotoxin

assay agent" (in contrast to it being undisputed in *Teva* that a reasonable jury could have found that ***all*** humanized anti-CGRP antagonist antibodies will treat headache). *See* EX1003, ¶¶61, 66-67, 71-73, 88-91, 96-122. *Teva*, 23-24. Instead, as in *Idenix Pharms. LLC v. Gilead Scis. Inc.,* 941 F.3d 1149, 1159 (Fed. Cir. 2019), the evidence here shows that a POSA would have to screen the possible mammalian-expressed proteins for their secretion and activity levels and "produc[e]" them together to confirm the requirements of challenged claims 1-9.

No species/example disclosed: Unlike in *Teva,* the '767 Application does not disclose ***any*** example of making an endotoxin assay agent comprising the three mammalian-expressed proteins having their respective activities. EX1017.

Not "routine" to complete the genus: Unlike in *Teva,* the evidence here demonstrates that a POSA would not deem it "routine" as of Dec. 10, 2013 to express all of the recited proteins (Factor C, B, and Pro-clotting enzyme) from all of the recited possible species of horseshoe crab, in all of the recited possible mammalian expression systems, to generate secreted (for Factor C) and functional proteins for use as an endotoxin assay agent. EX1003, ¶¶61, 71, 72, 89-92, 96-122. This evidence, along with the absence of any disclosed example, or any assertion of a structural feature common to all such combinations of proteins, counsels that *Teva* is inapplicable and that written description and enablement are lacking.

Respectfully submitted,

Date: June 1, 2026

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

I certify that on June 1, 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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