

Paper No. _____
Filed: March 16, 2026

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

HALOZYME, INC.,
Petitioner,

v.

ALTEOGEN, INC.
Patent Owner.

Case IPR2026-00176
Patent No. 12,221,638

PETITIONER'S OPPOSITION
TO PATENT OWNER'S DISCRETIONARY-DENIAL REQUEST

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I. INTRODUCTION

Petitioner Halozyme, Inc. pioneered methods for production of recombinant hyaluronidase PH20. Wei (EX1006) and Wei 2013 (EX1037) are examples of Halozyme's patent publications describing these innovations. EX1006, Cover; EX1037, Cover. Nearly a decade later, Alteogen decided to enter the U.S. market and pirate this technology. EX1001, Cover.¹ By its own admission in its Request for Discretionary Denial (RDD), all Alteogen did was tweak the second culturing temperature of Wei as instructed by similar temperature shift protocols in the prior art. Alteogen attempts to excuse its misappropriation of Halozyme's technology by mischaracterizing the petition challenge as cumulative. But Alteogen's attorney argument amounts to nothing more than smoke and mirrors.

First, there is no dispute that Zmuda (EX1005) is new prior art that was never considered during prosecution in any form and is directly on point. Zmuda, like multiple other prior art references not previously before the Office (e.g., Xu, Becerra), shows that the claimed temperature shift is soundly within what the prior art discussed. Zmuda also raises a presumption of obviousness based on overlapping ranges that was not implicated during prosecution or considered by the

¹ Halozyme promptly filed this challenge within weeks of the '638 patent being eligible for inter partes review.

Office. Moreover, Alteogen is in no position to contest its claims as anything beyond routine optimization (within prior art ranges) because its own patent claims broad ranges despite limited experimental data points.

Second, there is no credible dispute that Halozyme's Wei patent discloses every element of the challenged claims, with the sole exception of the second culturing temperature being 28-34°C (which is indisputably supplied by Zmuda). Indeed, Wei achieved all claimed enzyme properties using a substantially similar second culturing temperature of 35.5 °C. Accordingly, the dispute boils down to whether the difference between 34°C and 35.5°C falls squarely within the guidance provided by the prior art. As Zmuda capably demonstrates, it does.

Finally, Alteogen raises meritless "missing element" arguments that do not, in fact, identify any missing element. Instead, Alteogen primarily argues that the results in Wei (using limitations [1.1] and [1.3]) were achieved even at 35.5°C rather than 34°C. But this is nothing beyond poorly-disguised attorney argument to sidestep a presumption of obviousness—it is not a bona fide missing element argument. Ultimately, Alteogen does nothing more than attack the prior art individually and ignore the asserted obviousness rationale. All of Alteogen's criticisms fail.

II. PROCEDURAL BACKGROUND AND UNDISPUTED ERROR

Alteogen repeatedly acknowledges the claims were allowed because the

Examiner erroneously identified two claim elements missing from the art: (1) the second culturing temperature element [1.2] of 28-34°C; and (2) the enzymatic activity element [1.5] of 10,000 units/mL. RDD 4, 7. But the petition materials established, and Alteogen’s RDD does not dispute, that the asserted prior art discloses each of elements [1.2] and [1.5]. *See* RDD, Section Heading III (challenging only limitations [1.1] and [1.3]. Accordingly, material prosecution error is genuinely undisputed.

Indeed, the petition materials presented new prior art evidence disclosing a range overlapping with the claimed second culturing temperature range [1.2]. Pet. 1-3, 10-11. This is now undisputed. Alteogen also does not dispute that none of Zmuda, Xu, or Becerra were considered during prosecution—all are new references. The claimed temperature ranges fall squarely within and overlap with what is disclosed in the prior art, thereby creating a presumption of obviousness.

Reference	First Temperature	Second Temperature
Wei (EX1006)	37°C	less than 37°C (e.g., 35.5, 36.0, 36.5)
Zmuda (EX1005)	37°C	30 to less than 37°C (e.g., 32°C)
Xu (EX1012)	36.5°C	33 to 35°C
Becerra (EX1014)	37°C	28 to less than 37°C
Challenged Patent	35-38°C	28-34°C (e.g., 32°C)

The petition materials also demonstrated that Wei discloses producing

recombinant hyaluronidase protein satisfying all claimed physical properties. Pet. 2, 11-12. This too is now undisputed. Alteogen does not dispute that Wei's hyaluronidase satisfied both the sialylation percentage [1.4] and enzymatic activity [1.5] limitations of the claims. Alteogen even concedes that the failure of the prior art to teach methods for producing protein with this combination of properties was the basis for allowance. RDD 6 ("agreeing that second NOA reasons for allowance was based on 'combination' of activity and sialylation" (citing Pet. 11-12; EX1004, 8)). Furthermore, Alteogen never disputes that this prior art disclosure (of the combination of activity and sialylation in Wei) was never discussed by the Examiner. Alteogen also does not dispute that the Examiner turned instead to a different reference for enzymatic activity. RDD 4 ("25% sialic acid (sialylation) from Wei, incubation for 2 days at 30°C from Chen, and ***enzymatic activity from Frost.***").² Allowance was thus based on what is now an undisputed error—misapprehending the prior art hyaluronidase as lacking limitations [1.4] and [1.5].

III. THE PETITION PRESENTS MATERIALLY DIFFERENT ART AND ARGUMENTS

A. Alteogen's Attempt to Equate Zmuda to Chen Fails

Because Zmuda is indisputably a new reference that was never considered in

² All bold-italic emphases added unless otherwise indicated.

any form and that discloses a temperature shift protocol with the second culturing temperature limitation, Alteogen's entire §325 argument hinges on asserting that Zmuda is cumulative to Chen. RDD 9-12. But Alteogen's comparison fails for at least two reasons.

First, the petition advances a legal doctrine that was never applied by the Examiner during prosecution, but which should have been. Pet. 9-11. This matters because the claims were never subjected during prosecution to a presumption of obviousness based on an overlapping prior art range, as the law requires. Alteogen never presented evidence of criticality or unexpected results. Nor could it, considering the broad claims and limited data points in the specification.

Alteogen mischaracterizes a prosecution rejection as invoking overlapping ranges, whereas the rejection was issued over the teaching of Chen to employ a single data point—that is “incubation for **2 days at 30°C.**” RDD 10-11, 12-14 (emphasis in original). There was no discussion of prior art temperature ranges, and even Alteogen's own citation does not identify a **prior art range**. Nor does it identify any invocation by the Examiner of case law providing the presumption of obviousness when a claimed range overlaps with a **prior art range**. Alteogen certainly does not identify evidence that the Examiner applied a prior art second culturing range of “30 to less than 37°C,” as is disclosed in Zmuda. Pet. 2, 17.

Second, while Alteogen falsely equates Chen with Zmuda, they are

materially different. In addition to failing to identify any prior art range in Chen, Alteogen fails even to identify evidence that Chen teaches a temperature shift protocol (e.g., any “second” culturing temperature) at all. Alteogen cannot credibly do so, because it told the Examiner quite the opposite. EX1004, 39 (Alteogen stating “**Chen**, however, does not disclose or suggest...(2) *decreasing* the culture temperature to 28°C to 34°C and then culturing the host cells for 2 to 18 days, while maintaining the culture temperature....”). Alteogen’s arguments that Zmuda is cumulative to Chen are not only factually incorrect, but also are directly contradicted by Alteogen’s own statements during prosecution.

Alteogen bizarrely alleges that the combination of Wei and Zmuda is cumulative to the Examiner’s prior consideration of Wei. RDD 11 (citing Pet. 31). Two pages earlier in its brief, however, Alteogen argues the opposite—attacking Wei as lacking the claimed second 28-34°C temperature of limitation [1.2]. RDD 8. Alteogen argues here, and elsewhere in its RDD, that the Examiner allowed the claims believing this claimed second 28-34°C temperature was missing from Wei. Yet, Alteogen does not dispute—nor could it—that Zmuda (like several other newly cited references) clearly discloses the claimed second temperature range limitation [1.2] in a temperature shift protocol. Zmuda was not in front of the Examiner and no one claims otherwise. Even if both Wei and Zmuda additionally “provide good reason to optimize” within prior art ranges, as the law dictates, that

does not render Zmuda's admittedly new disclosure cumulative. As such, the combination of Wei and Zmuda is materially different from what the Examiner considered by Alteogen's own admission.

Even Alteogen acknowledges that §325(d) is not implicated unless the art and argument presented in the Petition are "at least substantially the same as the Examiner's." RDD 12. Because Alteogen's argument ignores the material differences between the art and argument presented by the Petition as compared to what was considered and applied during prosecution, its RDD should be denied.

B. Alteogen Does Not Argue Criticality

Alteogen falsely claims the "rationale to modify Wei" was already considered and traversed. RDD 12-14. Alteogen, however, offers little beyond internally inconsistent argument, similar to what is addressed above. Alteogen argues "the Examiner expressly considered routine experimentation and conventional teachings." RDD 13. But Alteogen's prosecution argument was premised on questioning the ability to achieve the claimed combination of "PH20 activity and sialylation levels" (RDD 13), which Wei indisputably achieved.³

³ Wei reported the hyaluronidase produced using the Gen2 method (e.g., Example 15) satisfied both the sialylation and enzymatic activity limitations. Pet. 35, 37; EX1006, Example 6 (testing the material from Example 15).

Alteogen's current argument thus merely underscores the error Alteogen invited by failing to inform the Examiner that Wei discloses the claimed combination of PH20 activity and sialylation, as discussed in further detail below.

Alteogen has never addressed, let alone rebutted, the presumed obviousness of its claims capturing temperature ranges of prior art protocols. Indeed, Alteogen is in no position to contest lack of criticality of its claimed ranges because its own patent relies on routine optimization and lack of criticality. Specifically, the patent broadly claims ranges of parameters, whereas only single data points, narrow disclosure, or no disclosure is provided in the specification.

For example, the claims recite the second culturing temperature range of 28°C to 34°C, but the working examples in the patent exclusively employ 32°C. EX1001, 17:41-42 ("shifted the culture temperature to 32°C"), 17:48-49 (same), 17:56-57 (same), 17:64-65 ("followed by shifting the culture temperature to 32°C"), 18:8-9 (same), 18:60-61 ("cultured at a decreased temperature of 32°C"), 19:28-29 ("temperature was shifted to 32°C"), 19:60-62 (same), 20:66-67 (same), 25:10-12 ("a lowered temperature of 32°C"); *see also* EX1002, ¶67.

Given the breadth of the claims in comparison to the limited disclosure, Alteogen cannot credibly assert criticality of its claimed range. Presumably, this is why Alteogen has introduced no evidence of unpredictability across the prior art range and has failed to rebut the presumption of obviousness based on routine

optimization within the prior art range.

C. Alteogen Ignores Material Error

Overlooking an unconsidered reference (e.g., Zmuda) that teaches the allegedly missing claim element is a material error that favors institution. *Tesla, Inc. v. Charge Fusion Techs., LLC*, IPR2025-00152, Paper 11, at 2-3 (June 12, 2025). As discussed above, Alteogen said Chen **does not** disclose the second culturing temperature range. EX1004, 39. But Alteogen does not dispute in its RDD that Zmuda satisfies this limitation. This material prosecution error warrants institution. *Tesla*, IPR2025-00152, Paper 11 at 2-3.

Overlooking material teachings of a reference that was considered or applied during prosecution also constitutes material error. *Ecto World, LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13, at 5-6 (May 19, 2025) (precedential) (material examination error to overlook “certain teachings in the prior art on the IDS”); *CSPC Pharmaceutical Group Limited v. Ipsen Biopharm Ltd.*, IPR2025-00505, Paper 11 (July 16, 2025) (examiner error to overlook disclosure of “critical limitations in the claims” in appendix and associated protocol of reference that was applied during prosecution).

Here, the Examiner relied on Frost for the enzymatic activity limitation because the Examiner was not aware that Wei’s recombinant protein satisfied every claimed physical property. RDD 4 (“25% sialic acid (sialylation) from Wei,

incubation for 2 days at 30°C from Chen, and ***enzymatic activity from Frost.***”).

Alteogen did not correct the Examiner’s error during prosecution. Pet. 9-10.

Alteogen does not dispute in its RDD that Wei satisfies the physical property elements ([1.4]-[1.5]). Overlooking that Wei’s recombinant protein satisfied the physical property elements warrants institution. *Eunsung Global Corp. v.*

Hydrafacial LLC, IPR2025-00445, Paper 14, at 3 (July 10, 2025) (“the patent examiner overlooked certain teachings in [examiner-considered prior art] that appear to disclose the allowable features of the claims. Discretionary denial is not appropriate for this reason.”) (cite omitted).

Institution is particularly warranted here, because the Office overlooked the teachings of a never-previously-considered reference, “and the combined teachings of” it together with a reference over which the claims were rejected during prosecution. *Microsoft Corp. v. Partec Cluster Competence Center GmbH*, IPR2025-00318, Paper 9, at 2-3 (June 12, 2025).

Lacking any valid basis to contest material prosecution error, Alteogen stoops to unsupported smears. RDD 6-9 (accusing Petitioner of “stealthily” employing “sleight of hand” by relying on protein produced in Wei with its temperature shift of 35.5°C because the upper limit in the claim is 34°C). As even Alteogen admits, however, the Petition was very clear that Wei’s example “discloses decreasing the temperature in a stepwise fashion to 35.5°C.” RDD 9

(quoting Pet. 30). Indeed, the petition materials were abundantly clear throughout that the temperature reduction exemplified in Wei was to 35.5°C and that Zmuda was relied upon as providing prior art disclosure of the temperature shift within the claimed range. *E.g.*, Pet. 11 (“Zmuda...exemplifies the temperature shift method for protein production in CHO cells at 32°C and discloses an overlapping range between 30°C and less than 37°C for recombinant protein production.”), 14 (“the claims are rendered unpatentable by one simple modification to Wei...simply extending Wei’s temperature shift from the exemplified 35.5°C to 34°C or below”), 15 (“Zmuda specifically discloses the temperature range of 30°C to less than 37°C, and exemplifies operation specifically at 32°C, squarely within the claimed range”).

The petition materials similarly were clear that the power of asserting Wei ***in combination*** with Zmuda is that “Zmuda, filed years after Wei, powerfully corroborates that the claimed temperature range is merely a routine subset of the temperature disclosed in the prior art at the critical date.” Pet. 15 (“The challenged patent simply takes what Wei did, and applies it in a commercially available ExpiCHO cell line, essentially following the manufacturer’s protocols that were also prior art. Zmuda...applies a temperature shift method for cell culture protein directly to the ExpiCHO cell line” using the overlapping range).

As explained at length above, prosecution error occurred by: (1) failing to

recognize that Wei's protein already satisfied all property limitations of the claims (leading the examiner to turn to Frost instead); and (2) failing to find and apply prior art (e.g., Zmuda) disclosing that the insubstantial difference between the second culturing temperature employed in Wei and that claimed by the '638 patent was presumed to be obvious based on prior art disclosure of an overlapping range. Alteogen's attempts to rewrite prosecution fail to remedy either error, each of which independently justifies institution.

IV. ALTEOGEN'S "MISSING ELEMENT" ARGUMENTS FAIL

Alteogen's alleged "missing element" arguments (RDD 15-20) amount to nothing more than smoke & mirrors, and improperly attack the prior art disclosures individually. For each element ([1.1] and [1.3], the petition materials point to specific prior art disclosure. Each time, identification of the disclosure as satisfying the claim limitation is supported by well-reasoned expert testimony that is corroborated by objective scientific literature. To the extent Alteogen raises any factual dispute, its dispute is premised only on uncorroborated attorney argument, which mischaracterizes the Petition and attacks a strawman.

A. Element [1.3]

Alteogen does not credibly contest that Wei discloses maintaining at least one of pH or glucose concentration within the recited ranges. Instead, Alteogen primarily asserts that Wei exemplified doing so while decreasing the second

culturing temperature to 35.5°C, as opposed to 34°C. RDD 18-19. Alteogen’s primary argument is thus not a true “missing element” argument, but an argument that a single prior art disclosure does not anticipate the claimed combination. Of course, anticipation is not a prerequisite for proving obviousness. *Compare* 35 U.S.C. §§102, 103.

Indeed, Alteogen does not contest prior art disclosure of the second culturing temperature range overlapping with the claimed range, thereby creating a presumption of obviousness for the claimed range. The petition materials demonstrated without rebuttal that the prior art discloses the second culturing temperature range that overlaps with the claimed range. Pet. 1-3, 10-11. In particular, the petition materials demonstrated that Zmuda “discloses the second culturing temperature range of ‘less than 37°C and greater than 30°C, less than 35°C and greater than 31°C, or at a temperature of 32°C.’” Pet. 31 (quoting EX1005, [0021]. Zmuda “exemplifies shifting from 37°C to a culturing temperature of 32°C in its ‘high titer’ and ‘max titer’ protocols.” Pet. 31 (quoting EX1005, 82, 88. Like Wei, Zmuda discloses using the temperature downshift “for 2 to 18 days.” Pet. 31 (citing EX1005, 81-82, 88). All of this is now undisputed.

Alteogen implies that Dr. Butler somehow testified that it was not obvious to employ prior art pH or glucose maintenance practices at 34°C. RDD 19-20 (citing EX1002, ¶¶31, 40, 43). Not so. Citing corroborating evidence, Dr. Butler testified

that the alternatively-recited glucose or pH maintenance limitations failed to distinguish the prior art because they were “typical” and “conventional.” EX1002, ¶31 (temperature shift was “conventional” upon achieving desired cell density), ¶¶40-41 (maintaining glucose at 4.5-6.5 g/L was “typical”), ¶¶42-43 (maintaining “typical” pH of 7-7.2 was “conventional”). Dr. Butler’s un rebutted testimony confirms the alternative limitations of pH or glucose maintenance recited in the claims merely recite normal parameters that are expressly disclosed in the prior art.

Alteogen next argues that the Petition case for pH or glucose maintenance disclosure in Wei is premised on expectations, assumptions, and capabilities rather than actual disclosure. RDD 19 (citing EX1002, ¶¶136, 137, 139, 141). But Alteogen again misses the mark.

As an initial matter, Alteogen does not dispute that the claim element is satisfied by either alternative of (1) maintaining glucose within the recited range during the second culturing or (2) maintaining a pH within a range from 6.8 to 7.2. Pet. 32; EX1002, ¶132; EX1001, Claims. Though the petition materials demonstrated that Wei combined its temperature shift (e.g. to 35.5°C) with “controlling **both** the solution pH and the glucose concentration,” controlling pH during the second culturing is independently sufficient to satisfy this element. Pet. 16 (citing EX1006, [0360], [0373]; EX1002, ¶53 (“Gen1 and Gen2 methods for producing rHuPH20 control both pH and glucose concentration.”)).

As the petition materials explain, Wei teaches culturing cells in a bioreactor at a pH “**set to 7.2** and further teaches sampling daily for ‘**pH verification**’ using the bioreactor instrumentation “that allows for **monitoring and control of pH**,” as was conventional and routine in the art. Pet. 34; EX1002, ¶141 (“Wei teaches culturing cells in a bioreactor at a pH set to 7.2 and further teaches sampling daily for ‘pH verification.’”); EX1006, [0360] (“parameters were...**pH: 7.2**....The reactor was **sampled daily for** cellcounts, **pH verification**”), [0373] (“The reactor was sampled daily for...**pH verification**”). Zmuda teaches using buffering agents that are optimal for buffering at physiological pH levels, including MOPS, HEPES, and phosphate. Pet. 34; EX1002, ¶143; EX1005, [0147]. Alteogen does not contest that a pH set to 7.2 “falls within the pH range of the claim,” and provides no explanation why the Board should ignore the express disclosure of the prior art. Nor does it contest that its own patent admits that the pH range of 7.2 ± 0.4 is “conventional.” Pet. 34; EX1002, ¶142; EX1001, 21:9-11, Table 2. Alteogen simply cannot credibly distinguish its claims from the prior art on the basis of pH maintenance. This alone provides sufficient basis to reject Alteogen’s alleged “missing element” argument.

Alteogen’s attack against the alternative glucose maintenance limitation fares no better. Using the data provided in Wei, Dr. Butler calculated the glucose concentration provided by feeding when the temperature was shifted down to

35.5°C. Pet. 32 (“Dr. Butler explains that the glucose concentration after each feed is about 2.1 g/L” in Example 13 and “1.4 g/L” in Example 15); EX1002, ¶¶134-135 (“Wei teaches maintaining the glucose concentration in an optimal range” by feeding glucose at “2.1 g/L” in Example 13 and “1.4 g/L” in Example 15).

Alteogen does not dispute that these feed concentrations fall within the broad range (0.001-4.5 g/L) that is claimed, or explain why this does not satisfy the claim.

Nor does Alteogen provide any reason to expect the glucose concentration to depart from the claimed range during the relevant time. As Dr. Butler explains, the fact that the cells did not die confirms that the lower end of the claimed glucose range (0.001 g/L) was satisfied. EX1002, ¶136. Alteogen does not dispute this.

As a factual matter, Alteogen also does not rebut Dr. Butler’s calculations that the starting and feeding concentrations over the relevant time did not exceed the claimed range during two days of the second culturing. EX1002, ¶¶137-139; EX1006, [0360], [0373] (“The addition of the feed media was observed to dramatically enhance the production of soluble rHuPH20 in the final stages of production.”). Nor does Alteogen dispute that the claimed glucose range is so broad (0.001-4.5 g/L) that it encompasses the “conventional” range (1.0-4.0 g/L) employed in the prior art via “sequential feeding.” Pet. 33; EX1002, ¶140.

Accordingly, Alteogen’s complaints about “expectations” fail to distinguish the claims over the prior art.

B. Element [1.1]

Alteogen similarly mischaracterizes the petition materials as relying on inherency or guessing to establish the IVCD limitation. RDD 15-17. That is flatly false. Alteogen supports its argument by crop-quoting declaration testimony out of context. There is no credible dispute that the prior art itself discloses achieving the recited cell density by virtue of the data presented therein.

As the petition materials explain, IVCD is the “area under the growth curve.” Pet. 29; EX1002, ¶110; EX1034, 887. Though Wei does not numerically report the area under the curve, it discloses the data from which the area under the curve is readily calculated. Pet. 29 (“Wei discloses cell density and growth rates from which the IVCD is calculated....”); EX1002, ¶¶112 (“This data [for HUA0420C in Table 19 of Wei] reveals that cells were inoculated at a concentration of 0.46×10^6 cell/mL and grew to a maximum cell density of 9.70×10^6 cell/mL by logarithmic growth with a doubling time of 23.5 hours.”).

Table 19. Monitoring data for cell culture, harvest, concentration and buffer exchange steps.				
Parameter	HUA0406C	HUA04010C	HUA0415C	HUA0420C
Time from thaw to inoculate 100 L bioreactor (days)	21	19	17	18
100 L inoculation density ($\times 10^6$ cells/mL)	0.45	0.33	0.44	0.46
Doubling time in logarithmic growth (hr)	29.8	27.3	29.2	23.5
Max. cell density ($\times 10^6$ cells/mL)	5.65	8.70	6.07	9.70
Harvest viability (%)	41	48	41	41

EX1006, Table 19 (excerpted, highlighting added). The Petition is thus not relying on an expert to “estimate” the limitation or “assume” an inherent property. The

limitation is disclosed in Wei by virtue of its data. Dr. Butler merely explains how a POSA would recognize the reference is disclosing the element.

Because of the breadth of the claimed IVCD range (20×10^6 to 120×10^6 cells x day/mL), Dr. Butler also explained that the IVCD disclosed in Wei satisfied the claim by day 6. Pet. 29; EX1002, ¶¶110-117. Though not required to demonstrate prior art disclosure of the element, Dr. Butler provided evidence-based reasoning explaining his estimate as to **when** the limitation was first satisfied. No estimation or assumption is required to determine **whether** it was satisfied—that disclosure is provided by the reference itself, as a POSA would have understood. Alteogen makes no showing that Dr. Butler’s calculation of the area under the curve from the disclosed data is inaccurate.

Focusing exclusively on mischaracterizing Dr. Butler’s testimony about Wei, Alteogen also fails to account for the entirety of the evidence presented. In addition to Wei, the petition materials noted that Dr. Butler’s calculations were corroborated by objective scientific literature. Pet. 29; EX1035, Example 7, Table 24. As Dr. Butler explained, the prior art literature used the same Gen2 method as in Wei in the same CHO cells, and “discloses values for viable cell density over time” confirming that Wei’s methodology satisfied the IVCD limitation by day 6, without requiring any estimations or assumption as to timing. EX1002, ¶¶118-120 (IVCD 23.58×10^6 cells x days/mL at 145 hours).

119. From the data included in Table 24 of Baker, I calculated the cumulative integral of viable cell density (IVCD) values using the standard trapezoidal integration formulation:

$$IVCD = \sum_{t_1}^{t_2} \left(\frac{VCD_1 + VCD_2}{2} \right) \cdot (t_2 - t_1)$$

Hours	VCD (x10 ⁵ /ml)	IVCD 10 ⁵ cells.hours/ml	IVCD 10 ⁶ cells.day/ml
0	4.7	0	0
24	8.9	163.2	0.68
50	19.3	529.8	2.21
76	36.7	1257.8	5.24
120	73.6	3684.4	15.35
145	84.3	5658.15	23.58
165	98.8	7489.15	31.20
190	95.3	9915.4	41.31
201	105	11017.05	45.90
214	95.9	12322.9	51.35

EX1002, ¶¶119-120 (excerpted, highlighting added). Alteogen provides no rebuttal to this corroborating evidence, having failed entirely to address it.

During prosecution, neither the Examiner nor Alteogen ever asserted that Wei fails to satisfy the IVCD limitation. Pet. 9-10; EX1004, 47 (rejection); EX1004, 38-39 (failing to contest Wei's disclosure of element [1.1]). This lack of dispute over Wei's disclosure of the IVCD limitation makes sense, because Alteogen never presented any evidence of criticality with respect to the broadly

recited (20×10^6 to 120×10^6 cells x day/mL) IVCD range.⁴ Alteogen thus has no foundation to distinguish the prior art based on cell density. Pet. 5, 22-23 (conventional to shift temperature after achieving expected cell density to balance out longevity and productivity); EX1002, ¶¶31-32; EX1014, 2; EX1012, 191; Pet. 28 (recited cell density was conventional); EX1035, Table 24; EX1002, 119. Alteogen's latest unsupported attorney-argument provides no reason to reject the well-reasoned and corroborated evidence and argument in the Petition.

V. CONCLUSION

Alteogen's misuse of the patent system to interfere with Halozyme's rights to market its ground-breaking recombinant hyaluronidase product should be stopped. Halozyme's petition is meritorious, Alteogen's request for discretionary denial is not. Alteogen's RDD should be denied.

⁴ Indeed, the specification presents **no** experimental data providing integral viable cell density. EX1001, 17:42-43 ("when the integral viable cell density reached a predetermined level"), 17:49-50 (same), 17:58-59 (same), 17:65-66 (same), 18:9-10, 18:61-62 ("when the integral viable cell density (IVCD) reached a shift range"), 19:30-31 ("when the integral viable cell density reached the change range,"), 19:62-63 (same), 20:67-21:1 (same).

Dated: March 16, 2026

Respectfully submitted,

/ Michael T. Rosato /
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VI. CERTIFICATIONS

A. Page Limit

I certify that this discretionary-denial opposition complies with the type-volume limitation of Rule 42.24 in view of Webpage, *Interim Director Discretionary Process*, §III.C.iii6 (“ For discretionary denial requests due after September 1, 2025, a petitioner’s opposition to the patent owner’s discretionary denial brief is limited to 20 pages ”).

B. Rule 42.6(e)(4) Certificate of Service

I certify that today this paper was served electronically on Alteogen’s counsel at mark.feldstein@finnegan.com; joshua.goldberg@finnegan.com; yoonhee.kim@finnegan.com; william.neer@finnegan.com; sarah.slone@finnegan.com. See Paper 6 (PO Mand. Not.).

C. Declaration

All statements in this certificate of service made of my own knowledge are true and all statements made on information and belief are believed to be true. I acknowledge that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. 1001) and may jeopardize the validity of this proceeding.

Respectfully submitted,

Dated: March 16, 2026

/ Michael T. Rosato /
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