

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

GENZYME CORPORATION and
AVENTIS INC.,

Plaintiffs,

V.

NOVARTIS GENE THERAPIES, INC.
and NOVARTIS PHARMACEUTICALS
CORPORATION,

Defendants.

C.A. No. 21-cv-1736 (RGA)

JURY TRIAL DEMANDED

REDACTED PUBLIC VERSION

FILED: August 4, 2023

**PLAINTIFFS' OPPOSITION TO DEFENDANTS' MOTION FOR LEAVE
TO AMEND THEIR ANSWER, DEFENSES, AND COUNTERCLAIMS**

TABLE OF CONTENTS

	Page
I. INTRODUCTION	1
II. BACKGROUND	1
A. The '542 Patent.....	1
B. The Notebook Data.....	5
C. Evidence of Intent.....	5
III. LEGAL STANDARD.....	5
IV. ARGUMENT	7
A. Novartis's Proposed Amended Answer Is Futile as Novartis Fails to Adequately Allege "But-For" Materiality.....	7
B. The Data Novartis Cites Fails to Support its Theory.....	11
C. Novartis's Proposed Amended Answer Fails to Allege Facts Sufficient to Support the Requisite Intent	16
D. Novartis's Unclean Hands Defense Is Futile.....	18
V. CONCLUSION.....	19

TABLE OF AUTHORITIES

	Page(s)
Cases	
<i>Analog Devices, Inc. v. Xilinx, Inc.</i> , No. 19-cv-2225, 2021 WL 466859 (D. Del. Feb. 9, 2021).....	10
<i>Ashcroft v. Iqbal</i> , 556 U.S. 662 (2009).....	6, 9
<i>Barry v. Stryker Corp.</i> , No. 20-cv-1787, 2023 WL 2733652 (D. Del. Mar. 20, 2023)	18
<i>Bayer Cropscience AG v. Dow Agrosciences LLC</i> , No. 10-cv-1045, 2012 WL 1253047 (D. Del. Apr. 12, 2012)	17
<i>In re Burlington Coat Factory Sec. Litig.</i> , 114 F.3d 1410 (3d Cir. 1997).....	6
<i>Collectis S.A. v. Precision Biosciences</i> , 883 F. Supp. 2d 526 (D. Del. 2012).....	16, 17
<i>Cephalon, Inc. v. Slayback Pharma Ltd. Liab. Co.</i> , No. 17-1154-CFC, 2019 WL 3497105 (D. Del. Aug. 1, 2019).....	6
<i>Corning Inc. v. Wilson Wolf Man. Corp.</i> , 569 F. Supp. 3d 920 (D. Minn. 2021).....	10
<i>Easton Tech. Prods, Inc. v. FeraDyne Outdoors, LLC</i> , No. 17-cv-1222, 2019 WL 1513463 (D. Del. Apr. 8, 2019)	18
<i>Exergen Corp. v. Wal-Mart Stores, Inc.</i> , 575 F.3d 1312 (Fed. Cir. 2009).....	6, 7, 16, 17
<i>Human Genome Scis., Inc. v. Genentech, Inc.</i> , No. 11-cv-6519, 2011 WL 7461786 (C.D. Cal. Dec. 9, 2011).....	19
<i>Int’l Bus. Machines Corp. v. Priceline Grp. Inc.</i> , No. 15-cv-137, 2017 WL 1349175 (D. Del. Apr. 10, 2017)	6
<i>Int’l Test Solutions v. Mipox Int’l Corp.</i> , No. 16-cv-791, 2017 WL 2118314 (N.D. Cal. May 16, 2017).....	17
<i>Invista North America S.a.r.l. v. M&G USA Corp.</i> , No. 11-cv-1007, 2013 WL 12304544 (D. Del. May 3, 2013)	9, 10, 16, 17

<i>Liqwd, Inc. v. L'Oreal USA, Inc.</i> , No. 17-cv-14, 2019 WL 10252725 (D. Del. Apr. 30, 2019)	10
<i>Ohio Willow Wood Co. v. Alps South, LLC</i> , 735 F.3d 1333 (Fed. Cir. 2013).....	7
<i>Recticel Automobilsysteme GMBH v. Automotive Components Holdings, LLC</i> , No. 10-cv-14097, 2011 WL 5307797 (E.D. Mich. Nov. 3, 2011).....	10
<i>Therasense, Inc. v. Becton, Dickinson and Co.</i> , 649 F.3d 1276 (Fed. Cir. 2011).....	6, 7, 16, 17
<i>In re Wands</i> , 858 F.2d 731 (Fed. Cir. 1988).....	9
<i>Wyeth Holdings Corp. v. Sandoz, Inc.</i> , No. 09-cv-955, 2012 WL 600715 (D. Del. Feb. 3, 2012).....	6, 7
Statutes	
35 U.S.C. § 101.....	8
35 U.S.C. § 112.....	8
35 U.S.C. §103.....	7
Other Authorities	
Rule 8.....	6
Rule 9(b)	<i>passim</i>
Rule 12(b)(6).....	6

I. INTRODUCTION

AAV particles, which are the subject of this dispute, tend to aggregate when stored even for short periods of time. Aggregation is highly undesirable and, therefore, the inventors of the '542 patent investigated, discovered, and then patented novel preparations designed to prevent aggregation of the particles in storage. Having examined the lab notebook underlying the invention, Novartis now wishes to add a claim for inequitable conduct, after the close of discovery, by way of a proposed amended answer (the "Proposed Amended Answer"). The trouble for Novartis is that there is no inequitable conduct and Novartis's proposed amendment fails to meet the requirements for pleading inequitable conduct. The pleading contains no facts in support of the contention that the PTO would have rejected the issued claims in light of additional information, and, therefore, Novartis has not pled materiality with the specificity required by Rule 9(b). Nor has Novartis pled scienter with the requisite support. While Novartis provides a lengthy discourse on the prosecution history, there is no meat on either prong, materiality and intent, of the defense. Even accepting Novartis's allegations as true, Novartis has failed to allege facts sufficient to reasonably infer but-for materiality and specific intent.

II. BACKGROUND

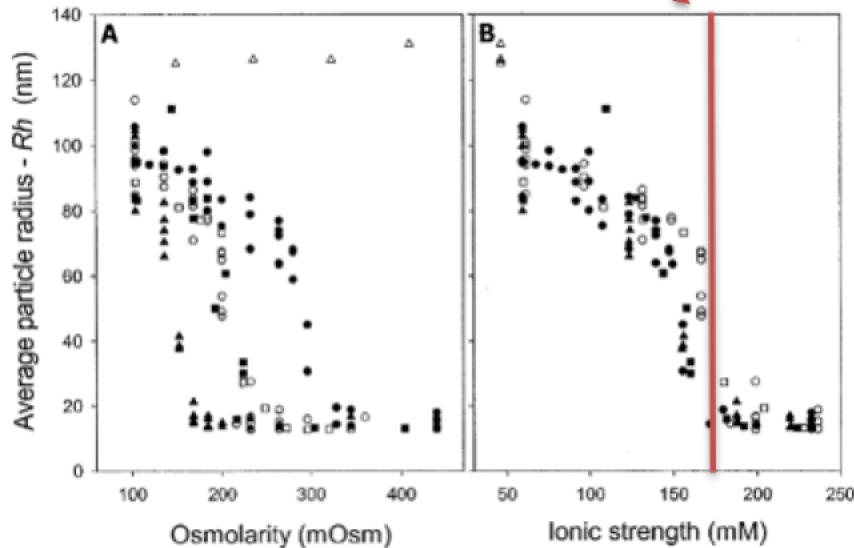
A. The '542 Patent

It is important in gene therapy to be able to deliver a sufficient dose of the AAV vector to the patient. Typical AAV particles are very small with an average radius of 13 nanometers (nm). D.I. 240, Ex. 1 ('542 patent), 1:37-48. But if those tiny particles aggregate, they can form significantly larger clumps that cause a host of problems, ranging from manufacturing losses and inconsistencies in purification, to biodistribution issues, to immunogenicity. *Id.*, 2:9-48. Aggregation gets worse as the concentration of viral particles in a formulation rises. *Id.*, 1:46-49.

Drs. J. Fraser Wright and Guang Qu discovered a solution to the aggregation problem. They discovered that certain combinations of formulations using a pH buffer in a narrow range, inclusion of specific ion groups, and an ionic strength above 200 mM (millimolar) would result in a better aggregation profile. Claim 1 of the '542 patent covers the basic formulation. *Id.*, cl. 1. Claim 5 further limits claim 1 to compositions where dynamic light scattering shows an average particle radius of “less than about 20 nm.” *Id.*, cl. 5. And claim 6 further limits the composition of claim 1 to those compositions which have a recovery of “about 90%” following filtration of the composition through a 0.22 µm filter. *Id.*, cl. 6.

The specification includes, among other things, the results of three sets of experiments on high ionic strength compositions. In Figure 1B, the specification states that “Fig. 1B demonstrates that vector aggregation is prevented when ionic strength is ~200 mM or greater regardless of which salt is used.” *Id.*, 7:20-22. The data shows a marked, cliff-like drop-off in aggregation once the ionic strength reaches a little below 200 mM.

Aggregation, as determined by average particle radius, drops significantly as ionic strength reaches 200 mM



The '542 patent also includes data from several other experiments, including a filtration experiment in which a filter is used to filter out aggregates. The results of those experiments appear in Table 2. *Id.*, 8:26-40.

TABLE 2

AAV VECTOR RECOVERY AT PROCESS SCALE					
Experiment	Formulation	μ (mM)	Target (vg/mL)	Actual (vg/mL)	Yield % (RSD)
1	CF	160	2.5E13	1.93E13	77 (6.6)
1	TF1	310	2.5E13	2.38E13	95 (7.4)
1	TF2	510	2.5E13	2.33E13	93 (7.4)
2	CF	160	6.7E13	3.98E13	59 (6.0)
2	TF2	510	6.7E13	6.42E13	96 (4.4)
3	CF (-Bz)	160	3.6E13	2.46E13	68 (11)
3	CF (+Bz)	160	3.6E13	3.29E13	91 (12)

The third column, “mM”, shows the ionic strength of the formulation. The last column, “Yield %” is a measurement taken after a filtration step designed to filter out clumped particles. The more particles caught in the filter, the lower the yield.

The '542 patent also describes experiments performed by the inventors whereby they assessed vector aggregation by conducting dynamic light scattering (DLS) testing at refrigerated conditions (4 degrees Celsius) and after various freeze-thaw cycles at -20 and -80 degrees Celsius. Given that the radius of a single particle is 13 nm, the closer the DLS reading is to that number the better. This data is reported in Table 3 (*id.*, 9:28-43):

TABLE 3

STABILITY OF AAV2 VECTORS

Formu- lation	Particle radius - Rh (nm)							
	4° C.		-20° C.			-80° C.		
	Pre	5 d	1 F/T	5 F/T	10 F/T	1 F/T	5 F/T	10 F/T
CF	14.5	27.0	22.4	56.1	94.5	20.6	57.5	141
TF1	13.8	16.3	TH	TH	TH	TH	TH	TH
TF2	13.8	14.4	14.2	14.0	14.1	13.8	21.3	50.9

Pre: DLS radius measured immediately following 0.2 µm filtration.
 Vector concentrations (vg/mL): CF: 1.93E13, TF1: 2.38E13, TF2: 2.33E13.
 TH: signal intensity is too high to measure because of extensive aggregation.

The data shows that the higher ionic strength concentrations TF1 (310 mM) and TF2 (510 mM) reported an average particle radius of 16.3 and 14.4 nm after five days of refrigerated storage, whereas the control formulation (160 mM) reported an average radius of 27 nm after 5 days. The specification notes that values above 20 nm indicate “the occurrence of some level of aggregation,” whereas values below 20 indicate that “no aggregation occur[red].” *Id.*, 9:19-54.

B. The Notebook Data

Novartis concedes that all of this supporting data was provided to the PTO but mounts its inequitable conduct challenge based on the failure to include in the final patent application two additional pieces of data. The first is data relating to a glycerol formulation, Experiment 25 in Laboratory Notebook 670¹, which had an ionic strength of 210 mM. D.I. 239, Ex. A ¶¶216-18.

Id., ¶219. The second set of allegations relates to the details regarding how certain filtration tests were conducted. *Id.*, ¶¶237-45.

C. Evidence of Intent

Novartis had the opportunity to depose both inventors Wright and Qu but cites to nothing in either deposition that would support an inference of intent to deceive. *See* D.I. 239, Exs. 2 & 7. Novartis did not even examine inventor Qu with respect to the matters at issue here. *See* D.I. 239, Ex. 7. All allegations relating to the prosecution attorneys are made on “information and belief” and are wholly unsupported by any facts. *See* D.I. 239, Ex. A ¶¶132-37, 140-41, 200-202, 242-43, 249, 254.

III. LEGAL STANDARD

To prove inequitable conduct, a challenger must demonstrate that a person having a duty of candor and good faith to the PTO withheld or misrepresented information that was but-for material to the examination of the patent application, and that this individual or individuals acted

¹ Genzyme does not dispute that Laboratory Notebook 670 was produced near the close of fact discovery and therefore does not assert that the defense should have been pled prior to the deadline for amending pleadings. On the other hand, Genzyme disagrees with Novartis's characterization of facts surrounding the production of the notebook. As explained in D.I. 249, Genzyme diligently searched for the relevant lab notebooks but could not find them. It turned out that the experiments performed by an inventor disclosed in the '542 patent were recorded in a notebook checked out to a non-inventor. When Genzyme discovered that fact, it promptly produced the notebook. Novartis had the notebook prior to both inventor depositions.

with the specific intent to deceive or mislead the PTO. *See Therasense, Inc. v. Becton, Dickinson and Co.*, 649 F.3d 1276, 1287-90 (Fed. Cir. 2011). “[T]o plead the ‘circumstances’ of inequitable conduct with the requisite ‘particularity’ under Rule 9(b), the pleading must identify the specific who, what, when, where, and how of the material misrepresentation or omission committed before the PTO.” *Exergen Corp. v. Wal-Mart Stores, Inc.*, 575 F.3d 1312, 1328 (Fed. Cir. 2009). This heightened pleading standard also applies to an unclean hands claim. *See Cephalon, Inc. v. Slayback Pharma Ltd. Liab. Co.*, No. 17-1154-CFC, 2019 WL 3497105, at *1 (D. Del. Aug. 1, 2019).

A district court may deny a motion requesting leave to amend if the proposed amendment is futile. *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1434 (3d Cir. 1997). “In assessing ‘futility,’ the district court applies the same standard of legal sufficiency as applies under Rule 12(b)(6).” *Id.* Although a court must accept as true the factual allegations in a pleading, the court is not obligated to accept legal conclusions as true. *Ashcroft v. Iqbal*, 556 U.S. 662, 664 (2009). Thus, even under Rule 8, “[t]hreadbare recitals of the elements of a cause of action, supported by mere conclusory statements, do not suffice.” *Id.* (citing *Bell Atlantic Corp. v. Twombly*, 550 U.S. 544, 555 (2007)).

“[A]t the pleading stage,” Novartis must “allege facts allowing for the reasonable inference of ‘but-for’ materiality.” *Wyeth Holdings Corp. v. Sandoz, Inc.*, No. 09-cv-955, 2012 WL 600715, at *6 (D. Del. Feb. 3, 2012), *adopted by*, 2012 WL 749378, at *1 (D. Del. Mar. 1, 2012); *see also Int’l Bus. Machines Corp. v. Priceline Grp. Inc.*, No. 15-cv-137, 2017 WL 1349175, at *10 (D. Del. Apr. 10, 2017) (“but-for materiality must be alleged in order to satisfy the materiality prong of inequitable conduct”), *adopted by*, 2017 WL 11549735, at *1 (D. Del. May 10, 2017). “But-for” materiality requires “proof that that the patentee withheld or

misrepresented information that . . . would have prevented a patent claim from issuing.” *Ohio Willow Wood Co. v. Alps South, LLC*, 735 F.3d 1333, 1345 (Fed. Cir. 2013). “A reasonable inference is one that is plausible and that flows logically from the facts alleged” *Exergen*, 575 F.3d at 1329 n.5. “Although inequitable conduct is conceptually broader than fraud, any such allegations must be pled in accordance with Rule 9(b), which requires that ‘the circumstances constituting fraud or mistake shall be stated with particularity.’” *Wyeth Holdings*, 2012 WL 600715, at *5. The requirement for particularity also applies to the proof of scienter. *Exergen*, 575 F.3d at 1328 (requiring “sufficient allegations of underlying facts” for a court to reasonably infer specific intent to deceive the PTO).

IV. ARGUMENT

A. Novartis’s Proposed Amended Answer Is Futile as Novartis Fails to Adequately Allege “But-For” Materiality

In the paradigm inequitable conduct case, the challenger asserts that a key piece of prior art known to the patentee was intentionally withheld from the PTO. Materiality arises from the fact that the art would have invalidated the claims under 35 U.S.C. §102 or §103. *See Therasense, Inc.*, 649 F.3d at 1291 (“prior art is but-for material if the PTO would not have allowed a claim had it been aware of the undisclosed prior art”). In other cases, the challenger seeks to prove that a statement made in a declaration filed with the PTO was false, in which case materiality is presumed. *Id.* at 1292 (where patentee files “unmistakably false affidavit, the misconduct is material”).

Here, Novartis presents a different sort of inequitable conduct theory and quite an unusual one. Novartis does not challenge any of the data in the patent but asserts instead that the inventor’s selection of data for inclusion in the patent application was so flawed as to render the patent unenforceable. By not disgorging the full contents of his lab notebooks, the inventors

stand charged with fraud and the lawyers who prosecuted the cases are accused of ethical violations “upon information and belief.” This type of claim is particularly subject to abuse because a defendant will always be able to point to *something* that the inventor or his lawyers elected not to include in a patent application. It is all the more important, therefore, that Novartis tie its theory carefully and methodically to the legal standard for materiality.

When subject to scrutiny, however, Novartis’s theory of materiality crumbles. All the Proposed Amended Answer states on the subject is that the PTO would have “rejected the claims” under 35 U.S.C. §§ 101, 112 or 103(a), or that the ’542 patent “would not have issued.” *See* D.I. 239, Ex. A ¶¶139, 144, 229, 255. The allegations are conclusory, and far more is needed to state a plausible claim.

The § 101 Theory

Other than a passing reference to § 101 in paragraph 144 of the Proposed Amended Answer, there is no discussion anywhere in the complaint as to how § 101 might apply to Novartis’s theory of inequitable conduct. *See* D.I. 239, Ex. A ¶144. The Proposed Amended Answer does not adequately put Genzyme on notice of the theory of the case with respect to § 101, much less meet the heightened pleading requirements for inequitable conduct.

The § 103 Theory

The Proposed Amended Answer also refers to § 103, asserting that the Examiner would have rejected the claims under that statute had the Examiner been aware of the additional data. *Id.*, ¶¶229-30. The Proposed Amended Answer does not explain why that is so by identifying the purported prior art disclosure and showing why it would have rendered the claims obvious. Indeed, it is difficult to see how § 103 could apply at all given that the data at issue was

confidential data generated by an inventor. Genzyme is not required to guess. The § 103 claim is futile as well.

The § 112 Theory

With respect to § 112, Novartis's Proposed Amended Answer does not attempt to allege *how* the withheld data relates to any relevant legal standard. *Id.* For example, while Novartis references "enablement" in paragraph 144 and section "112" in other paragraphs, Novartis's Proposed Amended Answer never explains how any of the omitted data demonstrates a lack of enablement. *Id.*, ¶¶144, 229-30. The specification discloses numerous formulations, with detail on the pH range to be used, the types of ions to be used, and the ionic strength of the formulations. Creating the formulations and testing for aggregation is trivial. Nor does the Proposed Amended Answer provide any factual allegations that would support an inference of lack of enablement under the *Wands* factors. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

Under similar circumstances, the Court in *Invista North America S.a.r.l. v. M&G USA Corp.*, No. 11-cv-1007, 2013 WL 12304544, at *14 (D. Del. May 3, 2013), *adopted by*, No. 11-cv-1007, D.I. 350 (D. Del. May 30, 2013) denied a motion for leave to add inequitable conduct claims and defenses. The Court held that the patent challenger had failed to plead a viable inequitable conduct defense as to one patent when the pleading included only "conclusory allegations that the withheld internal data is material, and that it contradicts disclosed data." *Id.* There, the Court pointed out that M&G presented no facts showing that if the data were presented to the PTO, that it would have rendered the invention unpatentable. *Id.* Moreover, the Court agreed that merely stating that the "PTO would not have granted the patent had it known of the omission or misrepresentation are insufficient because they are conclusory legal conclusions under *Iqbal*." *Id.* (quoting *Human Genome Scis., Inc. v. Genentech, Inc.*, No. 11-cv-

6519, 2011 WL 7461786, at *4 (C.D. Cal. Dec. 9, 2011). Much like the pleading in *Invista*, Novartis relies on conclusory legal assertions.² See, e.g., D.I. 239, Ex. A ¶¶139, 144, 229, 255; see also *Analog Devices, Inc. v. Xilinx, Inc.*, No. 19-cv-2225, 2021 WL 466859, at *3 (D. Del. Feb. 9, 2021) (conclusory allegation of “but for” materiality insufficient based on conclusory assertion that the “USPTO would not have granted one or more claims”) (Andrews, J.).

Other courts have consistently found conclusory allegations regarding but-for materiality to be insufficient. See *Corning Inc. v. Wilson Wolf Man. Corp.*, 569 F. Supp. 3d 920, 929 (D. Minn. 2021) (“the allegations fail to demonstrate why any of the allegedly withheld data would have rendered the claims unpatentable as they are merely conclusory in that regard”); see also *Recticel Automobilsysteme GMBH v. Automotive Components Holdings, LLC*, No. 10-cv-14097, 2011 WL 5307797, at *7 (E.D. Mich. Nov. 3, 2011) (finding allegations conclusory where counterclaim did “not contain sufficient factual allegations” alleging how the PTO would have “reject[ed] a claim in the patent application”); *Liqwd, Inc. v. L’Oreal USA, Inc.*, No. 17-cv-14, 2019 WL 10252725, at *19 (D. Del. Apr. 30, 2019) (“L’Oréal’s conclusory and speculative assertion that ‘the failure to disclose materials associated with click chemistry discussed above, at a minimum, caused the Examiner to give the declarations greater weight and ultimately allow the ’419 and ’954 patents,’ is insufficient to satisfy the heightened pleading standard under Rule 9(b).”).

² While the *Invista* Court found but-for causation adequately pled as to two other patents, the defendant’s pleading specifically explained how the “undisclosed test results” undercut an unexpected results argument which the “Examiner ultimately accepted.” *Invista*, 2013 WL 12304544, at *5, 9. Novartis’s Proposed Answer does not adequately explain how any of the undisclosed data in this case would have resulted in a 101, 103, or 112 rejection by the Examiner.

In summary, because Novartis has failed to explain why the data at issue would have prevented issuance, Novartis has failed to state a claim and the Proposed Amended Answer is futile.

B. The Data Novartis Cites Fails to Support its Theory

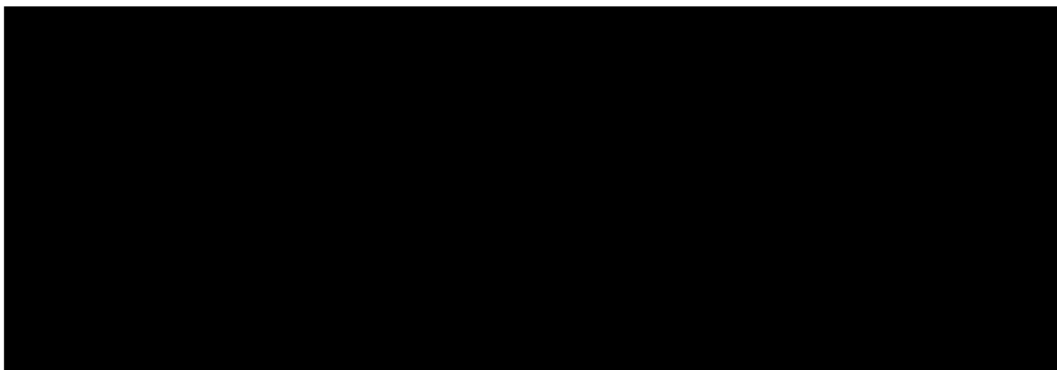
While the failure to tie the data to materiality is fatal, a closer look at Novartis's allegations shows that the Proposed Amended Answer is replete with error and exaggeration. Indeed, the actual data contradicts Novartis's position.

The Omitted Glycerol Formulation

Novartis claims that it was material to withhold data on Experiment 25 because the data

[REDACTED] D.I. 240 at 6. Novartis treats test results showing a 20 nm radius as the cutoff for preventing aggregation. *Id.* at 5. Yet, when explaining the data, Novartis admits that the DLS data was [REDACTED] D.I. 239, Ex. A ¶¶218-19.

Novartis provided the following chart (D.I. 239, Ex. A ¶218):



As shown above, and boxed in green, the glycerol formulation (identified FTF2) reported a hydrodynamic radius of [REDACTED] [REDACTED]

[REDACTED]³ *Id.*, ¶218. Thus, while Novartis's Proposed Amended Answer contains conclusory allegations that the 210 mM formulation (FTF2) [REDACTED] [REDACTED] the facts actually alleged show otherwise. *See id.* ¶¶219, 161, 247.

Aware of the problem with its theory, Novartis pleads that the data fails to show efficacy for an "extended period," but that is not a claim term, and it certainly does not refer to weeks or months in the context of the patent. The patentee used the phrase "extended period" to refer to the five-day data in Table 3 of the specification: "*As explained at page 20, second paragraph of the specification and in Table 3, recombinant AAV particles prepared and stored in elevated ionic strength solutions (greater than 200 mM as claimed) remain soluble with no aggregation and can be stored for an extended period.*" D.I. 240, Ex. 5 at 8 (emphasis added). The PTO determined that data showed no significant aggregation for a period long enough to support the issued claims. Novartis's Proposed Amended Answer and its briefing fail to explain *why* the Examiner would have rejected the claims when the [REDACTED]

[REDACTED] The theory has a logical hole at its core.

Novartis also points to the data from the freeze-thaw cycle testing (-20° C and -80° C) of the 210 mM formulation (Experiment 25), but the facts as pled by Novartis show that the [REDACTED]

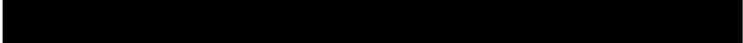
³ Claim 5 of the '542 patent is not limited to a particular timeframe of storage. While the DLS testing data [REDACTED]



As shown above, and as pled by Novartis, the 310 mM formulation reported aggregation after freeze-thaw cycling as “TH,” which means that the “[s]ignal intensity [is] too high to measure because of extensive aggregation.” D.I. 239, Ex. A ¶218, n.3. The 210 mM data is

 It is apparent that the PTO was not concerned about the freeze/thaw data – otherwise, it would have issued a rejection based on the “TH” data. There is no reasonable inference from the face of Novartis’s pleading that this data would have been but-for material to the patentability of any of the issued claims.

The Additional DLS Data

Novartis’s Proposed Amended Answer next alleges that additional hydrodynamic radius data for the 310 mM and 510 mM formulations, which are disclosed in the ’542 patent, also supports a finding of inequitable conduct. But Novartis’s allegations, on their face, concede that virtually all of the additional data  D.I. 239, Ex. A ¶218. The data, as pled by Novartis, does not reasonably raise the inference of but-for materiality.

[REDACTED]

As shown above, and boxed in green, all of the omitted day data, [REDACTED]

[REDACTED] Novartis

nevertheless alleges that [REDACTED]

[REDACTED] Mot. at 6.

As discussed above, “extended period” is not a claim term, and the statement in the file history was in the context of the five-day data reported in Table 3. There is nothing material about this data to the patentability of the ‘542 patent even taking Novartis’s own allegations as true.

The Measured Pre-Filtration Vector Concentrations

Novartis’s final inequitable conduct theory quibbles with how the filtration test was described to the Examiner. Claim 6 requires that the “recovery of the purified, recombinant virus particles is at least about 90% following filtration of the composition of said AAV vector particles through a 0.22 um filter.” D.I. 240, Ex. 1, cl. 6. Novartis points out that the percentage recovery calculations described in Table 2 of the ‘542 patent were based on the “[t]arget” concentration the inventors started with instead of the measurements gathered by the inventors right before the filtration step. D.I. 239, Ex. A ¶236. Novartis’s Proposed Amended Answer then alleges that the Examiner would have calculated different recovery percentages if Dr. Wright had disclosed the measured pre-filtration concentrations. *Id.*, ¶238. Table 2 of the ‘542 patent and Novartis’s calculations are shown here:

Table 2 of the '542 patent

TABLE 2

AAV VECTOR RECOVERY AT PROCESS SCALE

Experiment	Formulation	μ (mM)	Target (vg/mL)	Actual (vg/mL)	Yield % (RSD)
1	CF	160	2.5E13	1.93E13	77 (6.6)
1	TF1	310	2.5E13	2.38E13	95 (7.4)
1	TF2	510	2.5E13	2.33E13	93 (7.4)
2	CF	160	6.7E13	3.98E13	59 (6.0)
2	TF2	510	6.7E13	6.42E13	96 (4.4)
3	CF (-Bz)	160	3.6E13	2.46E13	68 (11)
3	CF (+Bz)	160	3.6E13	3.29E13	91 (12)

Paragraph 238 (D.I. 239, Ex. A)

Ionic Strength of Test Formulation	Identifying Nomenclature in '542 Patent, Table 2		Measured Post-Filtration Concentration	
160 mM	CF		1.93E13 vg/mL	
310 mM	TF1		2.38E13 vg/mL	
210 mM	<i>Omitted</i>		2.39E13 vg/mL	
510 mM	TF2		2.33E13 vg/mL	

As shown above and boxed in green, Paragraph 238 of Novartis's Proposed Amended Answer

concedes that the formulations with an ionic strength greater than 200 mM still [REDACTED]

[REDACTED] This alone

demonstrates that, if the Examiner had the data that Novartis complains of, each of the

formulations with ionic strengths greater than 200 mM [REDACTED]

[REDACTED] D.I. 240, Ex. 1,

cl. 6.⁴ This data still supports claim 6 and cannot be but-for material.

⁴ Importantly, claim 6 does not require that the formulation achieve 90% recovery relative to a formulation with less than 200 mM in ionic strength. See D.I. 240, Ex. 1, cl. 6. It simply requires that a formulation of claim 1, which can be stored without significant aggregation, achieve 90% recovery following 0.22 μ m filtration.

Novartis asserts that there is still inequitable conduct because the data regarding 0.22 μm filtration “did not reduce the amount of vector particles . . . *in comparison to a control formulation* with a lower-than-claimed ionic strength.” D.I. 239, Ex. A ¶247 (emphasis added). The 160 mM control formulation achieved 77% recovery when based on the target concentration (Table 2) and [REDACTED]

[REDACTED] But claim 6 does not require that the formulation achieve 90% recovery in comparison to a formulation with less than 200 mM in ionic strength. *See* D.I. 240, Ex. 1, cl. 6. Novartis’s argument imports a limitation into the claims which does not exist. The plain language of claim 6 simply requires that a formulation of claim 1, which can be stored without significant aggregation, achieve 90% recovery following 0.22 μm filtration.⁵ Even though the relevant data clearly supports claim 6, Novartis once again resorts to a conclusory allegation that the omission of data for the 160 mM control formulation—outside the scope of claim 6—was “material” and “tainted prosecution.” D.I. 239, Ex. A ¶244. This does not satisfy the heightened pleading standard.

C. Novartis’s Proposed Amended Answer Fails to Allege Facts Sufficient to Support the Requisite Intent

At the pleading stage, “a party must plead facts ‘from which the [c]ourt could reasonably infer that the patent applicant made a deliberate decision to deceive the PTO.’” *Invista*, 2013 WL 12304544, at *5 (*Wyeth Holdings Corp.*, 2012 WL 600715, at *6-9 (citing cases)). Novartis must allege “specific factual allegations” showing that specific individuals “decided to

⁵ Novartis’s Proposed Amended Answer also ignores that claim 6 requires both 90% recovery and storage without significant aggregation. As Novartis’s own pleading shows on its face, *see supra* at 12, even if the control formulation achieved over 90% recovery following 0.22 μm filtration, the control formulation still reported significant aggregation that was absent from the test formulations.

deliberately withhold it from the relevant examiner.” *Exergen*, 575 F.3d at 1331. The allegations must establish that the only reasonable inference from the record is intent to deceive, so that if there is more than one way to view the evidence, the claim fails. *Therasense*, 649 F.3d at 1290 (intent to deceive the PTO must be “the single most reasonable inference able to be drawn from the evidence.”).

Moreover, *Therasense* “dictated that materiality and intent must be evaluated separately” and that “intent cannot be solely inferred from materiality.” *Invista*, 2013 WL 12304544, at *11 (citing *Therasense*, 649 F.3d at 1290); see also *Cellectis S.A. v. Precision Biosciences*, 883 F. Supp. 2d 526, 534 (D. Del. 2012). Thus, even if Novartis has adequately alleged but-for materiality (it has not), Novartis “must offer some additional factual allegations regarding deceptive intent.” *Invista*, 2013 WL 12304544, at *11. In other words, there must be “some other evidence that indicates that the applicant appreciated the information’s materiality.” *Cellectis*, 883 F. Supp. 2d at 534.

Here, Novartis has failed to allege any specific factual allegations separate from its materiality assertions that would support an inference of intent to deceive. For example, Paragraph 145 of the pleading alleges that individuals had the “intent to deceive the PTO” with no factual support. Paragraph 200 states that information was “intentionally” omitted from the ’222 Provisional but does not allege that this was a deliberate decision to deceive the PTO or any facts to support such an allegation. The closest Novartis comes to alleging specific intent is Paragraph 230 of its Proposed Amended Answer where Novartis alleges that Dr. Wright and Mr. Bellomy “intended to deceive the PTO,” but the only support for this allegation is preceding Paragraph 229, which asserts that the undisclosed data would have been material to patentability.

Novartis's Proposed Amended Answer runs afoul of the *Therasense* rule: intent cannot be solely inferred from materiality. While Novartis correctly notes that intent can be inferred from indirect and circumstantial evidence, it is still required to plead facts which support the inference that Dr. Wright, Mr. Bellomy, and Ms. Robins deliberately attempted to deceive the PTO. Novartis has not done so. *See Bayer Cropscience AG v. Dow Agrosciences LLC*, No. 10-cv-1045, 2012 WL 1253047, at *5 (D. Del. Apr. 12, 2012) ("It is not reasonable to infer that Timmis had a specific intent to deceive the PTO simply because he did not reveal one aspect of the results published in his 1995 article" and "intent may not be inferred solely from materiality"); *Int'l Test Solutions v. Mipox Int'l Corp.*, No. 16-cv-791, 2017 WL 2118314, at *7 (N.D. Cal. May 16, 2017) ("intent to deceive cannot be inferred solely based upon failure to disclose known information, even if it is highly material"). The inequitable conduct allegations can be denied for this reason alone. *See Easton Tech. Prods, Inc. v. FeraDyne Outdoors, LLC*, No. 17-cv-1222, 2019 WL 1513463, at *7 (D. Del. Apr. 8, 2019) ("allegations do not allow the court to reasonably infer Mr. Palomaki had the requisite specific intent to deceive the USPTO" and "intent cannot be solely inferred from materiality"), *adopted by*, No. 17-cv-1222, D.I. 29 (D. Del. Apr. 26, 2019) (Andrews, J.). Accordingly, the Proposed Amended Answer fails to satisfy the pleading requirement for the intent to deceive element.

D. Novartis's Unclean Hands Defense Is Futile

Novartis's motion should also be denied with respect to its unclean hands defense. The unclean hands defense rests on the same facts that underlie the inequitable conduct counterclaim. An "unclean hands defense that depends on proof of fraud falls within the scope of the heightened Rule 9(b) standard." *Barry v. Stryker Corp.*, No. 20-cv-1787, 2023 WL 2733652, at *9 (D. Del. Mar. 20, 2023). Novartis's unclean hands defense rests on the same factual allegations as the inequitable conduct defense and should be dismissed for the same reasons. *See*

Human Genome Sciences, 2011 WL 7461786, at *8 (dismissing unclean hands defense where it “relies on the same facts . . . as it does for the inequitable conduct counterclaim”).

V. CONCLUSION

For the foregoing reasons, Defendants’ motion should be denied.

Dated: July 28, 2023

WILKS LAW, LLC

OF COUNSEL:

Katherine A. Helm
Noah M. Leibowitz
DECHERT LLP
Three Bryant Park
1095 Avenue of the Americas
New York, NY 10036
(212) 698-3500
khelm@dechert.com
noah.leibowitz@dechert.com

Martin J. Black
Sharon K. Gagliardi
DECHERT LLP
Cira Centre
2929 Arch Street
Philadelphia, PA 19104
(215) 994-4000
martin.black@dechert.com
sharon.gagliardi@dechert.com

Jonathan D.J. Loeb
DECHERT LLP
3000 El Camino Real
Five Palo Alto Square, Suite 650
Palo Alto, CA 94306
(650) 813-4800
jonathan.loeb@dechert.com

Amanda K. Antons
DECHERT LLP
35 W. Wacker Drive, Suite 3400

/s/ Scott B. Czerwonka

David E. Wilks (Del. Bar # 2793)
Scott B. Czerwonka (Del. Bar # 4844)
4250 Lancaster Pike, Suite 200
Wilmington, DE 19085
(302) 225-0858
dwilks@wilks.law
sczerwonka@wilks.law

*Attorneys for Plaintiffs
Genzyme Corporation and Aventis Inc.*

Chicago, IL 60601
(312) 646-5800
amanda.antons@dechert.com