IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

RAVGEN, INC., Plaintiff, v. ARIOSA DIAGNOSTICS, INC., ROCHE SEQUENCING SOLUTIONS, INC., ROCHE MOLECULAR SYSTEMS, INC., and FOUNDATION MEDICINE, INC., Defendants.	)	C.A. No. 20-1646-RGA-JLH
RAVGEN, INC., Plaintiff, v. MYRIAD GENETICS, INC. and MYRIAD WOMEN'S HEALTH, INC., Defendants.	)	C.A. No. 20-1730-RGA-JLH
RAVGEN, INC., Plaintiff, V. BIORA THERAPEUTICS, INC., Defendant.	)	C.A. No. 20-1734-RGA-JLH

REPORT AND RECOMMENDATION

Before the Court are the parties' disputes over the construction of claim terms in United States Patent Nos. 7,727,720 (the "'720 patent"), and 7,332,277 (the "'277 patent"). The Court held a *Markman* hearing on May 31, 2023 ("Tr __."), and announced its recommendations from the bench on June 1, 2023. I recommend that the Court adopt the constructions set forth below.

	Term	**Court**
1	"agent that [inhibits cell lysis to inhibit the lysis of cells / inhibits lysis of cells / impedes cell lysis] . . . wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor" / "an agent that impedes [or inhibits] cell lysis" ('277 patent, claims 8, 55, and 81; '720 patent, claim 1)	"a substance that inhibits the lysis of cells that is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor, and does not include EDTA nor endogenous substances"
2	"cell lysis inhibitor" ('277 patent, claims 8, 55, and 81; '720 patent, claim 1)	"chemical substance that prevents the lysis of cells or preserves the structural integrity of cells"
3	"membrane stabilizer" ('277 patent, claims 8, 55, and 81; '720 patent, claim 1)	"chemical substance that stabilizes the membranes of cells"
4	"free fetal DNA isolated" / "isolating free fetal nucleic acid" ('277 patent, claims 55 and 81)	"free fetal DNA separated from non-nucleic acid" / "separating free fetal nucleic acid from non-nucleic acid"
5	"non-cellular fraction" ('720 patent, claim 1)	"portion that is substantially free of cells"

I. LEGAL STANDARDS

A. Claim Construction

The purpose of the claim construction process is to "determin[e] the meaning and scope of the patent claims asserted to be infringed." *Markman v. Westview Instruments*, *Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). When the parties have an actual dispute regarding the proper scope of claim terms, their dispute must be resolved by the judge, not the jury. *Id.* at 979. The Court only needs to construe a claim term if there is a dispute over its

meaning, and it only needs to be construed to the extent necessary to resolve the dispute. *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999).

"[T]here is no magic formula or catechism for conducting claim construction." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1324 (Fed. Cir. 2005). But there are guiding principles. *Id.*

"The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation." *Id.* at 1313. In some cases, the ordinary meaning of a claim term, as understood by a person of ordinary skill in the art, is readily apparent even to a lay person and requires "little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314. Where the meaning is not readily apparent, however, the court may look to "those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean." *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004). Those sources include "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.*

"The claims themselves provide substantial guidance as to the meaning of particular claim terms." *Phillips*, 415 F.3d at 1314. For example, "the context in which a term is used in the asserted claim can be highly instructive." *Id*. Considering other, unasserted, claims can also be helpful. *Id.* "For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314–15.

In addition, the "claims must be read in view of the specification, of which they are a part." *Id.* at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). The specification "is always highly relevant to the claim construction analysis." *Id.* (quoting *Vitronics*, 90 F.3d at 1582). The specification may contain a special definition given to a claim term by the patentee, in which case, the patentee's lexicography governs. *Id.* at 1316. The specification may also reveal an intentional disclaimer or disavowal of claim scope. *Id.* However, "even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (internal marks omitted).

Courts should also consider the patent's prosecution history. *Phillips*, 415 F.3d at 1317. It may inform "the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.* Statements made by a patentee or patent owner during inter partes review may also be considered. *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1362 (Fed. Cir. 2017).

In appropriate cases, courts may also consider extrinsic evidence, which "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman,* 52 F.3d at 980. For example, dictionaries, especially technical dictionaries, can be helpful resources during claim construction by providing insight into commonly accepted meanings of a term to those of skill in the art. *Phillips*, 415 F.3d at 1318. Expert testimony can also be useful "to ensure that the court's understanding of the

technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.*; *see also Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 331–32 (2015).

B. Indefiniteness

Section 112 of Title 35 imposes a definiteness requirement on patent claims. 35 U.S.C. § 112(b) (requiring that the claims "particularly point[] out and distinctly claim[] the subject matter which the inventor . . . regards as the invention"). "The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, *e.g.*, competitors of the patent owner, can determine whether or not they infringe." *All Dental Prodx, LLC v. Advantage Dental Prod., Inc.*, 309 F.3d 774, 779–80 (Fed. Cir. 2002).

"A patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014). Definiteness, like claim construction, should be assessed from the viewpoint of a person of ordinary skill in the art at the time the patent was filed, and it should be considered in view of the patent's specification and prosecution history. *Id.* at 908.

The party asserting indefiniteness has the burden to prove it by clear and convincing evidence. *BASF Corp. v. Johnson Matthey Inc.*, 875 F.3d 1360, 1365 (Fed. Cir. 2017).

II. THE COURT'S RULING

My Report and Recommendation regarding the disputed claim terms of the '277 and '720 patents was announced from the bench on June 1, 2023, as follows:

I'm prepared to issue a report and recommendation on the claim construction disputes that were argued yesterday, May 31, 2023. The parties resolved a number of the briefed disputes before the hearing yesterday. To the extent that the parties agree on those constructions or any other constructions, they should file a proposed order for Judge Andrews's signature.

With respect to the terms that are still in dispute, I will not be issuing a separate written report and recommendation. I want to emphasize that, while I'm not issuing a separate written report and recommendation, we have followed a full and thorough process before making the recommendation that I'm about to state.

There was full briefing on each of the disputed terms. The parties submitted their briefing in accordance with my procedures, so each side had the opportunity to submit two briefs, and they were combined into one joint claim construction brief incorporating all arguments. The parties' joint claim construction chart and brief also included numerous exhibits with intrinsic and extrinsic evidence, including expert declarations. My oral ruling will cite to the evidence cited by the parties that I conclude best supports my proposed constructions, but my failure to cite to other evidence provided by the parties does not mean that I ignored or failed to consider it.

I'm not going to read into the record my understanding of the general legal principles of claim construction. I set forth the legal standards in my opinion in *3Shape v. Align*,[1] and I incorporate that articulation by reference. Defendants have also argued that several of the disputed terms are indefinite. My understanding of the law of indefiniteness is also set forth in *3Shape v. Align*.[2]

The first set of disputes comprise the majority of the parties' claim construction briefing. These disputes pertain to claims 8, 55, and 81 of the '277 patent and claim 1 of the '720 patent. Each of those four claims has an "agent" phrase with a similar format. Claim 8 of the '277 patent, for example, requires "an agent that inhibits cell lysis to inhibit the lysis of cells . . . wherein the agent is selected from a group consisting of membrane stabilizer, cross-linker and

[1] *3Shape A/S v. Align Tech., Inc.*, No. 18-886, 2020 WL 2188857, at *1–2 (D. Del. May 6, 2020), *report and recommendation adopted*, 2020 WL 7695898 (D. Del. Dec. 28, 2020).

[2] *Id.* at *2–3.

cell lysis inhibitor." Breaking that phrase down, it requires "an agent that inhibits cell lysis" where the agent is selected from a group of three things. The first is a membrane stabilizer. The second is a cross-linker. The third thing the agent that "inhibits the lysis of cells" can be is a cell lysis inhibitor.

Claim 55 has a similar format for the agent phrase. It requires "an agent that inhibits lysis of cells" where the agent is selected from the group of the same three things. Claim 81 is similar and requires "an agent that inhibits cell lysis" where the agent is selected from the group of three things. And finally, claim 1 of the '720 patent similarly requires "an agent that impedes cell lysis" where the agent is selected from the group of three things.

The parties have a number of sub-disputes relating to this agent phrase. In the first sub-dispute, Defendants say that two of the three things on the list of possible agents—the terms "cell lysis inhibitor" and "membrane stabilizer"—are indefinite because they are not terms of art and because the specifications do not provide guidance for a POSITA to determine whether a particular substance qualifies as one of those types of agents. I find that, on this record, Defendants have failed to demonstrate by clear and convincing evidence that those terms are indefinite.

As for "membrane stabilizer," Plaintiff says that a POSITA would understand it to mean "a chemical substance that stabilizes the membranes of cells." I recommend adopting that construction. It is consistent with the claim language. It is also consistent with the extrinsic declaration of Plaintiff's expert who says that the list of exemplary membrane stabilizers in the specification are chemical substances known to a POSITA as being capable of stabilizing the membrane of cells and that a POSITA reading that list would understand that a membrane stabilizer is a chemical substance that stabilizes the membrane of cells.[3]

I also note that my conclusion that the term "membrane stabilizer" has not been shown to be indefinite is consistent with the conclusion reached by Judge Albright in the *Ravgen v. Quest* case

[3] (No. 20-1646, D.I. 151, Ex. P3 ¶¶ 54–59.) All docket citations are to No. 20-1646 unless otherwise noted.

in Texas.[4] While his determination is, of course, not binding on this Court, I do agree with his conclusion.

Turning to "cell lysis inhibitor," Plaintiff's brief proposed construing it as a chemical substance that preserves the structural integrity of cells. To the extent that Plaintiff's proposed construction limits the mechanism by which the claimed agent has to inhibit cell lysis, I think that definition is too narrow. Nothing in the claim language suggests that the claimed cell lysis inhibitor has to inhibit cell lysis by a particular mechanism. Likewise, the specification does not suggest that the inhibition has to operate through a particular mechanism. Plaintiff's expert points out that some of the items on the list of cell lysis inhibitors set forth at column 31, lines 4–21 of the '277 patent, as well as Table XXIII beginning in column 226; and column 31, lines 43–54 of the '720 patent, as well as column 32 line 65 to column 33 line 28, and Table XXIII beginning in column 216, operate by preserving the structural integrity of the cells by cross linking.[5] But that is not a reason to import a cross-linking limitation into the term "cell lysis inhibitor," and doing so would not be consistent with another portion of the specification at column 91, lines 46–49 that says that "any agent that prevents the lysis of cells or increases the structural integrity of cells can be used." In other words, the specification does not limit the cell lysis inhibitor to those agents that work by a particular mechanism.

During the hearing, I asked Plaintiff's counsel if, consistent with that portion of the specification, the "cell lysis inhibitor" could instead be construed as a chemical substance that prevents the lysis of cells or preserves the structural integrity of cells. Counsel agreed.[6] Accordingly, I agree with Plaintiff that Defendants haven't demonstrated indefiniteness, and I recommend that "cell lysis inhibitor" be construed as "a chemical substance that prevents the lysis of cells or preserves the structural integrity of cells."

Before I turn to the next sub-dispute, I'll make a few comments about Defendants' arguments on indefiniteness.

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[4] *Ravgen Inc., v. Quest Diagnostics, Inc.*, No. 20-972, D.I. 65 at 5–6 (W.D. Tex. Oct. 5, 2021) (D.I. 151, Ex. P14).

[5] (D.I. 151, Ex. P3 ¶¶ 48–53.)

[6] (Tr. 72:25–75:2.)

Defendants recognize that a claim limitation defined by its function is not necessarily indefinite, but Defendants argue that a POSITA wouldn't be able to determine if a given agent was a cell lysis inhibitor or a membrane stabilizer. I don't take Defendants to be arguing that a POSITA couldn't test an agent to see if it inhibits cell lysis or stabilizes cell membranes, and, in fact, the specification provides an example of such a test for inhibition of cell lysis. Instead, Defendants' real point appears to be a that the claimed "membrane stabilizer" and "cell lysis inhibitor" are very broad and that a person of skill could not determine *ex ante* if a compound inhibits cell lysis under particular conditions. However, as the Federal Circuit explained in the *BASF* case, breadth is not indefiniteness.[7] Moreover, as the Federal Circuit explained in the *Nevro* case, definiteness does not require that a potential infringer be able to determine *ex ante* if a particular act infringes the claims.[8]

Plaintiff's expert opines that a POSITA reading the specifications and claims would have understood how to determine whether an agent is a membrane stabilizer or a cell lysis inhibitor.[9] Taking into account that extrinsic evidence and the intrinsic evidence, I find that, on this record, Defendants have failed to demonstrate that a POSITA could not determine whether a particular agent is a cell lysis inhibitor or a membrane stabilizer.

I also reject Defendants' argument that, in order for the claims to be definite, the specification or claims need to specify how much lysis inhibition or membrane stabilization is required. In a similar argument, some, but not all, of the Defendants argue that the terms "membrane stabilizer" and "cell lysis inhibitor" are terms of degree that fail to provide objective boundaries to a POSITA. I reject that argument because I disagree that the terms are terms of degree.

As Defendants point out, the list of items in the Markush group overlap; that is, a certain substance may be both, for example, a cell lysis inhibitor and a cross-linker. Moreover, the Court's proposed construction of "cell lysis inhibitor" to include any chemical substance that inhibits cell lysis means that the "cell lysis

[7] *BASF Corp. v. Johnson Matthey Inc.*, 875 F.3d 1360, 1367 (Fed. Cir. 2017).

[8] *Nevro Corp. v. Boston Scientific Corp.*, 955 F.3d 35, 40 (Fed. Cir. 2020).

[9] (D.I. 151, Ex. P3 ¶¶ 42–59.)

inhibitor" species in the Markush group is essentially as broad as the genus "agent that inhibits cell lysis." Defendants agreed at the hearing, however, that the mere overlap does not result in indefiniteness, and I agree with them on that.[10] I'm not aware of any case that says that a Markush group expression is indefinite if its species overlap or even if a particular species is coextensive with its genus. It seems to me that if a POSITA could understand the bounds of the term regardless of the overlap, they are not indefinite.[11]

Defendants also point out that a particular agent might operate as a membrane stabilizer or cell lysis inhibitor under certain conditions but not others. I do not think that makes those terms indefinite. As I already noted, the definiteness inquiry does not require that a POSITA be able to determine *ex ante* if a particular agent falls within the scope of the claims, and I agree with Plaintiff that there's no requirement in the claims or the intrinsic record that the agent must stabilize cell membranes in every possible chemical environment in order to qualify as a membrane stabilizer or cell lysis inhibitor.

Another sub-dispute has to do with the word "lysis." Plaintiff's proposed construction substitutes the word "rupture" in for "lysis." Defendants say that's inappropriate. Defendants' argument is hard to follow, but they seem to be arguing that even if cells ruptured, that would not necessarily increase the ratio of maternal to fetal DNA if a nuclear membrane in the cell is intact. Here is what I will say about this dispute: the extrinsic evidence does indeed suggest that "cell lysis" means the same thing as the "rupture of cells," but I don't understand at this point how replacing one word for another resolves any dispute for the parties or would clarify anything for the jury. The parties are free to bring this up at a later stage in the case if it appears that it's going to have a material impact. For now, we'll leave it as "lysis."

The next set of sub-disputes have to do with Plaintiff's proposal that the Court construe the agent phrase to exclude

[10] (Tr. 41:23–42:5.)

[11] (D.I. 151, Ex. P14 at 4–5 (*citing Lexington Luminance LLC v. Amazon.com, Inc.*, 601 F. App'x. 963, 968 (Fed. Cir. 2015) ("Definiteness involves more than an examination of the technical correctness of the use of a *Markush* expression that may have slipped past the examining process. It involves evaluation of the claim in light of the written description.")).)

"chelators used as anticoagulants" and "endogenous substances." I'll take "endogenous substances" first. I agree with Plaintiff that the agent phrase is not met by "endogenous substances." Construing the agent term to be met by something that's already in the blood sample is contrary to the intrinsic evidence, and I don't think the cited portions of the prosecution history support Defendants' argument. I also note that this same argument was rejected by Judge Albright in the *Ravgen v. Natera* case, and I agree with his reasoning and conclusion.[12]

The last sub-dispute is Plaintiff's proposal to entirely exclude from the agent phrase "chelators used as anticoagulants." On this dispute, I do not entirely agree with Plaintiff or with Judge Albright. Plaintiff's argument goes like this: the specification contains an example experiment in which the test sample was treated with the cell lysis inhibitor formaldehyde in an EDTA tube, and the control sample was put in an EDTA tube. The control experiment was referred to in the example as having been analyzed "in the absence . . . of inhibitors of cell lysis." ('277 patent, 89:1–34.) This suggests that the patentee did not consider EDTA to be an inhibitor of cell lysis in this experiment. EDTA is not included in the exemplary lists of cell lysis inhibitors, membrane stabilizers, and cross-linkers in the specification of either patent.

During prosecution of the '277 patent, the examiner rejected certain claims as anticipated by Lo, stating, "Lo et al. teach collecting maternal blood into a tube comprising EDTA (i.e. an agent that inhibits cell lysis."[13] The patentee responded in pertinent part:

> In addition to being improperly supported by documentary evidence, the assertion by the Office that EDTA is a cell lysis inhibitor is simply incorrect. Applicant asserts that EDTA is not an "agent that inhibits cell lysis." Rather, EDTA is a well-known chelator of calcium and magnesium. EDTA is routinely added to blood during the blood collection process as an anticoagulant due to its ability to chelate calcium. In fact, EDTA is sometimes

[12] *Ravgen, Inc. v. Natera, Inc.*, No. 20-692, D.I. 176 at 6–8 (W.D. Tex. Nov. 8, 2021) (D.I. 151, Ex. P5).

[13] (D.I. 151, Ex. P6 at 5.)

> included as an ingredient in cell lysis buffers. . . . EDTA is clearly referred to as a chelator in Applicant's specification, not as a cell lysis inhibitor. . . . As shown in Example 4, discussed above, the addition of formalin, even in the presence of EDTA, to samples has a dramatic effect on the amount of free fetal DNA isolated from the samples. The fact that the addition of formalin can have such a dramatic effect on the percentage of free fetal DNA serves to demonstrate that formalin and EDTA have very different properties and cannot be equated to each other.
>
> Since Lo et al. does not teach or suggest the use of an agent that inhibits cell lysis, Lo et al. does not teach and every element of [the rejected claims] . . . and since the Office's assertion that EDTA is a cell lysis inhibitor is wholly unsupported by documentary evidence or reasoning, the rejection of [the claims] is improper.[14]

Plaintiff further points out that at various points during the prosecution of the asserted patents, the examiner treated references as not having disclosed the claimed agent notwithstanding the fact that when one goes back and looks at those references, they teach addition of the compounds EDTA and ACD, both of which are anticoagulant chelators. According to Plaintiff, this intrinsic evidence makes clear that anticoagulant chelators cannot be an agent that inhibits cell lysis or a cell lysis inhibitor. Judge Albright accepted that argument, as did the PTAB in one of the IPRs.[15]

Defendants say that, at best, the intrinsic evidence shows that the patentee disavowed coverage of EDTA as a "cell lysis inhibitor" but that EDTA could still be an "agent that inhibits cell lysis" if it, in fact, performed that function in a particular product or reference.

I agree with Plaintiff and the PTAB to the extent they conclude that the patentee disclaimed coverage of EDTA as a cell

[14] (D.I. 151, Ex. P7 at 33.)

[15] *Ravgen, Inc. v. Natera, Inc.*, No. 20-692, D.I. 176 at 4–5 (D.I. 151, Ex. P5); *Illumina, Inc. v. Ravgen, Inc.*, No. IPR2021-01271, D.I. 45 at 15–23 (P.T.A.B. Jan. 25, 2023) (D.I. 169, Ex. 2).

lysis inhibitor and an agent that inhibits cell lysis. The patentee's statements in the prosecution history demonstrate a clear disavowal of EDTA as a cell lysis inhibitor and an agent that inhibits cell lysis.

But I disagree with Plaintiff and the PTAB to the extent that they conclude that the disclaimer extends more broadly to other anticoagulant chelators. The only clear disavowal in the prosecution history is the disavowal of EDTA.

I don't think the specification supports Plaintiff's argument that anticoagulant chelators cannot be the claimed agent. If anything, the specification suggests that anything can be the claimed agent if it has the effect of inhibiting cell lysis. For example, at column 91 lines 48–49, it says, "Any agent that prevents the lysis of cells or increases the structural integrity of cells can be used." The specification is also clear that the claimed cell lysis inhibitor and membrane stabilizers are "not limited to" the chemicals listed in the specification. Plaintiff points out that EDTA is referred to in the specification as a chelator, but there is nothing in the specification that suggests that chelators in general cannot be the claimed agent. Rather, the specification is clear that anything that inhibits cell lysis can be the claimed agent.

In sum, I conclude that the genus phrase should be construed as "a substance that inhibits the lysis of cells that is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor, and does not include EDTA nor endogenous substances."

"Cell lysis inhibitor" should be construed as "chemical substance that prevents the lysis of cells or preserves the structural integrity of cells." And "membrane stabilizer" should be construed as "chemical substance that stabilizes the membranes of cells."

The next set of disputed terms are the isolating terms. The parties briefed a dispute about the phrase "isolating free nucleic acid" which appears in claim 1 of the '720 patent. I'm not sure that there was a real dispute there that needed resolution, and at the hearing, the parties appeared to have agreed. They're going to meet and confer and propose a construction to the extent appropriate.

However, there remains a dispute about the phrases "free fetal DNA isolated," which appears in claim 55 of the '277 patent; and "isolating free fetal nucleic acid," which appears in claim 81 of

the ’277 patent. The essence of the dispute between the parties is the question of what the fetal DNA has to be isolated or separated from. Defendants say the phrase requires the fetal DNA to be separated from non-nucleic acid materials and the maternal DNA. Plaintiff says the fetal DNA is separated from nonnucleic acid components, but it doesn’t have to be isolated from the maternal DNA.

While the language of the claims, read in isolation, might suggest that the fetal DNA has to be separated from all of the rest of the components of a sample, it’s not unambiguous on that point. Certainly, the claim does not say that the fetal DNA has to be separated from the maternal DNA.

Read in view of the specification, I am persuaded that the disputed phrases require separation of the fetal DNA from the non-nucleic acid components of the sample but that there is no requirement that it be separated from the maternal DNA. As Plaintiff points out, every example in the specification uses isolation techniques that do not separate the free fetal DNA from the free maternal DNA, so Defendants’ proposal would exclude every example in the specification.

I’ve also examined the portions of the prosecution history cited by Defendants in support of their construction. However, I agree with Plaintiff that the prosecution history indicates that the word “fetal” was added to the claims not to specify that the fetal DNA needs to be isolated from the maternal DNA, but rather to indicate that the analysis is performed on a sample obtained from a pregnant female that contains fetal DNA.[16]

I also note that my recommendation is consistent with the construction adopted by Judge Albright in the *Ravgen v. Labcorp* case.[17] While his construction is, of course, not binding on the Court, I do agree with his conclusion.

[16] (D.I. 83, Ex. 8 at 10, 25.)

[17] *Ravgen, Inc. v. Laboratory Corporation of Am. Holdings*, No. 20-969, D.I. 62 at 3–6 (W.D. Tex. Oct. 5, 2021) (D.I. 151, Ex. P19).

For these reasons, I recommend adopting Plaintiff's alternative proposal,[18] which resolves the actual dispute between the parties. "Free fetal DNA isolated" should be construed as "free fetal DNA separated from non-nucleic acid" and "isolating free fetal nucleic acid" should be construed as "separating free fetal nucleic acid from non-nucleic acid."

The final remaining disputed term is "non-cellular fraction." That term is found in claim 1 of the '720 patent. Plaintiff's proposed construction is "portion that is substantially free of cells." Defendants propose "a fraction that does not contain cells."

The dispute between the parties is whether "non-cellular fraction" must be entirely free of cells or instead substantially free of cells.

I agree with Plaintiff. Starting with the language of the claims, Defendants say it supports them because the word "non-cellular" means "no cells." I don't think it's as clear as Defendants suggest. The claims don't say no cells. They say "non-cellular fraction," and I'm not persuaded that the phrase "non-cellular fraction" means a fraction that contains absolutely no cells. A person reading this patent might also reasonably interpret the phrase "non-cellular fraction" to mean the fraction of the sample that is not the cellular fraction. But just because a fraction is not a cellular fraction does not mean it can't contain any cells.

Turning to the specification, there is nothing that requires or suggests that a non-cellular fraction is entirely devoid of cells. Moreover, one of the examples in the specification relating to isolating plasma from cells is consistent with Plaintiff's proposal that "non-cellular fraction" refers to a fraction substantially free of cells. ('720 patent, 211:11–26.)

As for the prosecution history, I agree with Plaintiff that there is no disclaimer or estoppel. Instead, the prosecution history reflects that the phrase "non-cellular fraction" was added to

[18] Plaintiff argued that no construction was necessary but offered an alternative proposal in case the Court construed the term. Plaintiff's alternative proposal clarifies how the Court has resolved the parties' dispute over this term and should therefore be adopted.

distinguish a prior art reference that isolated DNA from a cellular fraction.[19]

And that concludes my report and recommendation.

This Report and Recommendation is filed pursuant to 28 U.S.C. § 636(b)(1)(B),(C), Federal Rule of Civil Procedure 72(b)(1), and District of Delaware Local Rule 72.1. Any objections to the Report and Recommendation shall be filed within fourteen days and limited to ten pages. Any response shall be filed within fourteen days thereafter and limited to ten pages. The failure of a party to object to legal conclusions may result in the loss of the right to *de novo* review in the district court. The parties are directed to the Court's "Standing Order for Objections Filed Under Fed. R. Civ. P. 72," dated March 7, 2022, a copy of which can be found on the Court's website.

Absent any objections, the parties shall file a Proposed Order consistent with this Report and Recommendation for the Court's approval.

Dated: July 10, 2023

The Honorable Jennifer L. Hall
United States Magistrate Judge

[19] (D.I. 152, Ex. P54 at 2, 9, 13.)