IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CHROMADEX, INC. and TRUSTEES OF DARTMOUTH COLLEGE,

Plaintiffs,

v.

ELYSIUM HEALTH, INC.,

Defendant.

C.A. No. 18-1434-CFC

REDACTED - PUBLIC VERSION

JOINT CLAIM CONSTRUCTION BRIEF

HIGHLY CONFIDENTIAL – ATTORNEY'S EYES ONLY

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LIST OF ABBREVIATIONS

- **"The Asserted Patents"** refers to U.S. Patent Nos. 8,383,086 and 8,197,807.
- **"ChromaDex"** refers to Plaintiff ChromaDex, Inc.
- **"Dartmouth"** refers to Plaintiff Trustees of Dartmouth College.
- **"Elysium"** refers to Defendant Elysium Health, Inc.
- **"NR"** refers to nicotinamide riboside.
- **"POSA"** refers to a Person of Ordinary Skill in the Art
- **"PTAB"** refers to the Patent Trial and Appeal Board.
- **"The '086 patent"** refers to U.S. Patent No. 8,383,086, attached as Exhibit B to the Joint Appendix.
- **"The '807 patent"** refers to U.S. Patent No. 8,197,807, attached as Exhibit A to the Joint Appendix.
- **"The -1795 IPR"** refers to *Elysium Health Inc. v. Trustees of Dartmouth College*, No. IPR2017-01795 (PTAB).
- **"The -1796 IPR"** refers to *Elysium Health Inc. v. Trustees of Dartmouth College*, No. IPR2017-01796 (PTAB).

I. INTRODUCTION AND BACKGROUND

A. ChromaDex's Opening Position

The Asserted Patents are directed to compositions containing nicotinamide riboside ("NR"), a unique form of vitamin B3 that increases cellular metabolism, mitochondrial function, and energy production. The inventor, Dr. Charles Brenner, while a faculty member at Dartmouth, discovered that isolated NR provides an independent and previously unknown route to the production in humans of "NAD+," a coenzyme vital to cellular function. Although other forms of vitamin B3 were known, Dr. Brenner discovered that isolated NR could be formulated and administered orally in a way that enhances NAD+ biosynthesis more effectively than those other forms of vitamin B3, while also avoiding undesirable side effects. Dr. Brenner's discoveries resulted in the Asserted Patents, which are assigned to Dartmouth.

ChromaDex was the third company to license the Asserted Patents, but the first to successfully commercialize NR. After spending millions of dollars ensuring that NR is both safe and efficacious for human consumption, ChromaDex began selling commercial batches of NR in 2014 to companies that market direct-to-consumer products. One of those companies was a start-up, Elysium.

Elysium bought NR from ChromaDex for inclusion in its consumer product called "BASIS®," the same product now accused of infringing the Asserted Patents.

Notably, during the time Elysium was purchasing NR from ChromaDex, it was aware of the Asserted Patents and marked them on the label of its BASIS product. Elysium, however, wanted the NR market all to itself, and not long after its commercial relationship with ChromaDex began, it set upon a course to "destroy" ChromaDex and "take control of everything." D.I. 63-1, Ex. A at 232, 249. Using the financial chaos that Elysium itself caused by ordering large amounts of NR from ChromaDex that it never intended to pay for, Elysium approached Dartmouth and tried to steal away ChromaDex's exclusive license to the Asserted Patents. The private text messages made public in the California Action make this crystal clear, with Elysium's principals discussing their "game changing" patent strategy and exclaiming "We need those patents!" *Id.* at 250; Ex. 1 at 133.

When Elysium was unable to obtain a license to the Asserted Patents, it filed two IPRs trying to invalidate them. Elysium challenged the '807 Patent in the -1796 IPR, but the PTAB denied institution because it found that Elysium had "not established a reasonable likelihood of prevailing" on any of its challenges. Ex. 2 at 12. Elysium challenged the '086 patent in the -1795 IPR, but was again unsuccessful, with the Board concluding in its Final Written Decision that Elysium had "not shown by a preponderance of the evidence that claim 2 is" invalid. Ex. 3 at 42.

Elysium knew that its BASIS product infringed the Asserted Patents and that it could avoid liability only by obtaining a license to the Asserted Patents from

Dartmouth or by invalidating them. It achieved neither. Now, in a renewed attempt to avoid liability for its willful infringement, Elysium offers unreasonable and implausible claim-construction arguments that are completely inconsistent with years of Elysium's own conduct and understanding of what the Asserted Patents cover. The Court should not countenance Elysium's tactics.

B. Elysium's Answering Position

Plaintiffs' introduction betrays the many shortcomings in their claim construction arguments. Rather than focus on the objective exercise before the Court—correct construction of disputed claim terms—Plaintiffs devote nearly all their space to unproven allegations and personal attacks having nothing to do with claim construction.

Plaintiffs' statement is rife with misstatements, claiming, for example, that Dr. Brenner discovered that NR enhances NAD+ biosynthesis "more effectively than … other forms of vitamin B3" while "avoiding… side effects." This is palpably untrue, as evidenced by the specification. It lacks disclosure of any testing (comparative or otherwise) of the effects of NR in any species of animal. Also false is Plaintiffs' assertion that Elysium's IPR proceedings were "unsuccessful." The PTAB invalidated more than half the claims Plaintiffs asserted in their complaint, including all but one claim of the '086 patent.

Turning to the actual issues before the Court, Plaintiffs' claim construction arguments ignore the intrinsic record, contradict Dartmouth's own statements to the Patent Office, and misapply Federal Circuit precedent. Plaintiffs assert that their constructions reflect the understanding of a POSA but, tellingly, they do not support these assertions with an expert declaration.

To support their arguments, Plaintiffs are forced to walk back material admissions Dartmouth made during the IPR proceedings or in the original prosecution that contradict the broad claim constructions Plaintiffs now propose. For example, in response to Elysium's IPR petition Dartmouth explained that "from a natural or synthetic source" in claim 2 of each Asserted Patent ***excluded*** chemically-synthesized NR. Now, wanting to prove infringement by Elysium's chemically-synthesized NR product, Plaintiffs reverse course, urging the Court to construe claim 2 more broadly to cover exactly that.

Plaintiffs' proposed construction of the '807 patent also flies in the face of Dartmouth's statements to the Patent Office during prosecution. The '807 patent claims a composition comprising "isolated nicotinamide riboside ***in combination with*** one or more of tryptophan, nicotinic acid, or nicotinamide" (emphasis added). Dartmouth added this limitation during prosecution to overcome the "Tanimori" reference, cited in the patent as teaching chemical synthesis of NR. Dartmouth argued that Tanimori did not teach an NR composition "formulated" by "combining"

the isolated NR with tryptophan, nicotinic acid, and/or nicotinamide, "as presently claimed." Ex. 10 at 4-5.

Plaintiffs' problem: Elysium's accused product is not formulated by combining NR with tryptophan, nicotinic acid, or nicotinamide. Their solution is to argue that the words "in combination with" require no more than that one of the added components—nicotinamide, for example—be "found in" the ultimate composition, even if no combination ever occurred. Plaintiffs omit that nicotinamide is necessarily "found in" every composition of NR, because nicotinamide is a degradation product of NR, and it also is present as an impurity when NR is chemically synthesized, such as in Tanimori's process. Dartmouth added the "in combination with" limitation for the very purpose of differentiating the claimed combination composition from Tanimori's chemically-synthesized NR. Plaintiffs' construction of "in combination with" as meaning only "found in"—making the term synonymous with "comprising"—effectively reads the limitation out of the claim.

Plaintiffs also seek to add arbitrary limitations unsupported by the claim language or specification to avoid their central Section 101 problem: NR is a product of nature found in cow's milk. Attempting to differentiate the claimed NR compositions from naturally-occurring NR compositions to avoid subject matter ineligibility, Plaintiffs ask the Court to engraft a 25% purity requirement on the term

"isolated NR," contrary to the specification's express definition of an "isolated molecule," which contains no level of purity requirement.

Plaintiffs' efforts to stretch the claims to cover Elysium's accused product should be rejected. The Court should adopt Elysium's constructions, which are faithful to the claim language, the specification, and the prosecution history.

C. ChromaDex's Reply Position

Continuing its years-long attempt to avoid the consequences of its willful infringement, Elysium proposes claim constructions that lack any basis in the meaning of the claim terms or the intrinsic evidence, and that are instead baldly aimed at avoiding infringement. For example, relying on assertions by its expert Dr. Adams, Elysium attempts to redefine the term "nicotinamide riboside" to include NR esters that do not include the defined structure of NR and that have different properties than NR. For the "isolated" terms, Elysium takes the nonsensical position that NR isolated from the products of a chemical synthesis is not NR isolated from a "synthetic source," even though a chemically synthesized product mixture that includes NR is, by definition, a "synthetic source" of NR—indeed, it is hard to

imagine what a synthetic source for NR could be, aside from the products of a chemical synthesis.[1]

For the "in combination with" term, Elysium again relies on its expert's assertions to advance a construction that departs from the term's plain meaning and impermissibly imports a process step into a composition claim. Finally, Elysium's proposed constructions of "increases NAD+ biosynthesis upon oral administration" and "pharmaceutical composition" impermissibly read embodiments into the claims instead of following the terms' plain meaning, contrary to well-established Federal Circuit precedent.

D. Elysium's Sur-Reply Position

The Court will observe several themes in Plaintiffs' arguments:

They repeatedly attempt to disavow claim construction positions Dartmouth advocated in prosecution and IPR proceedings. These are not just a co-plaintiff's prior inconsistent statements, they are the statements of the applicant, made in

[1] Elysium's attempt to confuse the meaning of "isolated" here is particularly inappropriate, given that the PTAB's Final Written Decision, affirmed by the Federal Circuit, expressly turned on the distinction between the naturally synthesized mixture containing NR (milk) and isolated NR (removed from the milk). Elysium points to no suggestion that "isolated" has a different meaning when NR is isolated from the products of a chemical synthesis rather than a naturally occurring one.

formal, written submissions to the USPTO to overcome rejections and avoid invalidity findings.

They consistently ignore language in the specification to rely on extrinsic evidence. They even go so far as to invite the Court to rely on Elysium manufacturing documents, created years after the patents' priority date, to construe the claims to cover the accused product. This is improper under claim construction law.

They make unsupported assertions about the supposed understanding of a POSA, based on attorney argument instead of an expert declaration. These assertions must be disregarded. Notably, Dartmouth's expert in the IPR, Dr. Zhaohui Zhou, attended last month's deposition of Elysium's claim construction expert, yet Plaintiffs elected not to submit an expert declaration in rebuttal.

Elysium's positions, supported by the intrinsic and extrinsic record and grounded in the understanding of a POSA as of the priority date, should be adopted.

II. DISPUTED TERMS

A. "nicotinamide riboside"

TERM (PATENT/CLAIMS)	CHROMADEX'S[2] PROPOSED CONSTRUCTION	ELYSIUM'S PROPOSED CONSTRUCTION
"nicotinamide riboside" '807 Patent: Claims 1 and 2 '086 Patent: Claim 2	No construction necessary. The term should be construed according to its plain and ordinary meaning.	"nicotinamide riboside or a derivative (e.g., L-valine or L-phenylalanine esters) of nicotinamide riboside"

1. ChromaDex's Opening Position

"Nicotinamide riboside" is a chemical compound with a defined structure that has a plain and ordinary meaning to a POSA. A POSA would understand "nicotinamide riboside" to refer to that chemical structure and hence encompass compounds containing the structure, such as nicotinamide riboside base and salts thereof. *See Allergan Sales, LLC v. Sandoz Inc.*, C.A. No. 12-CV-207 (JRG), 2016 WL 1224868, at *9 (E.D. Tex. Mar. 29, 2016) ("the Court construes the term 'brimonidine' according to its plain and ordinary meaning, the chemical compound brimonidine, including both its free base and salt forms"). No construction of this term is necessary.

[2] Plaintiffs ChromaDex and Dartmouth will hereinafter be referred to collectively as "ChromaDex."

Elysium proposes to construe "nicotinamide riboside" to mean "nicotinamide riboside or a derivative (e.g., L-valine or L-phenylalanine esters) of nicotinamide riboside." By defining "nicotinamide riboside" by reference to itself, Elysium implicitly acknowledges that "nicotinamide riboside" is well understood and needs no construction.[3] But Elysium's proposal goes on to expand the claim to cover additional compounds that do not contain nicotinamide riboside. Although the specification discloses that "the nicotinamide riboside *can be* a derivative (e.g., L-valine or L-phenylalanine esters) of nicotinamide riboside," '807 patent, 28:63-65,[4] and that "the present invention *also encompasses*" these same derivatives, *id.*, 29:4-8, these disclosures merely explain that the invention *can comprise* derivatives of NR exemplified by its L-valine or L-phenylalanine esters. But the claims recite "nicotinamide riboside"—not these esters or similar derivatives of NR that do not retain the chemical structure of NR—and the specification does not define NR to

[3] The fact that Elysium's proposed construction defines "nicotinamide riboside" by reference to itself also renders the proposed construction circular and potentially confusing. *See Triplay, Inc. v. Whatsapp, Inc.*, C.A. No. 13-1703 (LPS)(CJB), 2016 WL 3574012, at *15 (D. Del. June 30, 2016), *report and recommendation adopted*, C.A. No. 13-1703 (LPS)(CJB), 2016 WL 6778215 (D. Del. Nov. 15, 2016) ("TriPlay ended up with a proposed construction that includes the very term to be construed … , a circular result that is disfavored.").

[4] Unless otherwise noted, all emphases are added.

include them.[5] Thus, there is no support for Elysium's attempt to depart from the claims' plain and ordinary meaning. *See Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365-66 (Fed. Cir. 2012) ("To act as its own lexicographer, a patentee must 'clearly set forth a definition of the disputed claim term' other than its plain and ordinary meaning." (quoting *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002))).

2. Elysium's Answering Position

The specification provides that "***the nicotinamide riboside can be*** a derivative (e.g. L-valine or L-phenylalanine esters) of nicotinamide riboside." '807 patent at 28:63-65 (emphasis added). The patentee chose to define "nicotinamide riboside" to include derivatives; that choice must be honored. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1321 (Fed. Cir. 2005) (en banc) ("[T]he specification 'acts as a dictionary when it expressly defines terms used in the claims….'"). Elysium's construction adopts the express definition. Based on that definition, a POSA would understand nicotinamide riboside, in light of the specification, to mean nicotinamide riboside or

[5] As discussed above, a POSA would understand "nicotinamide riboside" to encompass the compound itself and salts thereof, which retain the chemical structure of NR. To the extent a salt of NR could be considered a "derivative" of NR, the term "nicotinamide riboside" includes such derivatives. Nonetheless, there is no support for Elysium's position that the term "nicotinamide riboside" includes derivatives that do not contain NR.

a derivative (e.g., L-valine or L-phenylalanine esters) of nicotinamide riboside. *See* Ex. 12 at ¶¶ 10-18.

Plaintiffs assert that no construction is necessary.[6] Their own arguments, proposing multiple competing constructions, belie that position. First, they argue that nicotinamide riboside has a "defined structure that has a plain and ordinary meaning to a POSA." *Supra*, at 9. They do not state what this "defined structure" is, nor do they provide any evidence of what a POSA would understand it to be. At the same time, they argue that ***some*** derivatives of nicotinamide riboside—specifically nicotinamide riboside salts—are within the scope of the claims. *Supra* at 9, 10 n.5. Their brief provides no support for why a POSA would understand the claim to encompass salt derivatives and no others.

Plaintiffs cannot have it both ways. Either nicotinamide riboside is limited to the positively-charged NR molecule or it encompasses derivatives. Plaintiffs are not free to cherry-pick one kind of derivative (the salt form) while excluding other derivatives. Plaintiffs would have the Court interpret "nicotinamide riboside" to include salt derivatives while excluding the L-valine and L-phenylalanine esters that the specification specifically provides "the nicotinamide riboside can be."

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[6] Construction is necessary to determine, for example, (1) whether the patent has fully enabled and described the genus of claimed NR compounds; and (2) whether particular NR derivatives (such as the NR-chloride salt used in ChromaDex's and Elysium's products) are within the claims.

Plaintiffs' arguments also are scientifically incorrect. First, there is no single "defined structure" of nicotinamide riboside. As explained by Elysium's expert Dr. Adams, the positively-charged nicotinamide riboside molecule can form two anomers (an α-anomer and a β-anomer) which have different structures, as taught by references cited in the specification. Ex. 12 at ¶¶ 8, 11-12.

Plaintiffs' assertion, unsupported by expert opinion, that a POSA would understand "nicotinamide riboside" to include only salt derivatives is also wrong. As Dr. Adams explains, a POSA would understand that the positively-charged nicotinamide riboside molecule could be derivatized in multiple ways, including both ester and salt forms. Ex. 12 at ¶ 13. As noted, the specification specifically provides that the nicotinamide riboside "can be" ester forms. Finally, contrary to Plaintiffs' claim that salts "contain the structure" of NR, salts of nicotinamide riboside, such as nicotinamide riboside chloride, are different chemical molecules than nicotinamide riboside. *See* Ex. 12 at ¶¶ 15-16.[7]

[7] Plaintiffs' reliance on *Allergan Sales, LLC v. Sandoz Inc.*, 2016 U.S. Dist. LEXIS 41013 (E.D. Tex. Mar. 29, 2016) is misplaced. The *Allergan* court, interpreting a different patent, based its opinion on factors unique to that case, including claim differentiation and specific language in the specification. *Id.* at *23-27. *Allergan* did not create a blanket rule that all claims to a molecule cover salts of that molecule.

3. ChromaDex's Reply Position

Elysium proposes to construe "nicotinamide riboside" to include "derivative[s] (e.g., L-valine or L-phenylalanine esters) of nicotinamide riboside." But Elysium's expert conceded that, unlike NR salts, the recited NR esters are unstable (unless made into a salt) and do not contain the defined structure of NR, which "[m]akes the molecule very different" from NR in a way that has "an enormous impact" on its properties. Ex. 28, 91:19-92:1, 97:5-99:1. Moreover, the specification does not *define* NR to include esters, but rather treats them as distinct. Elysium's proposed construction should therefore be rejected.

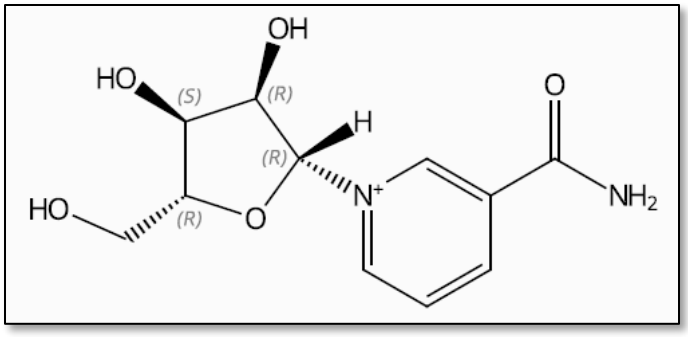
a. Elysium's Expert Conceded that NR Salts Are Suitable for Oral Administration, but NR Esters (Unless Made into a Salt) Are Not

Dr. Adams testified that "[a] stable chemical compound can have no overall charge," Ex. 12, ¶13, but that the NR molecule "is positively charged," *id.* ¶9. Thus, "for the positively-charged nicotinamide riboside to be administered to a patient, it necessarily would be derivatized so as to be overall electrically neutral." *Id.* ¶13. One way to make NR electrically neutral is by "creating salts" of NR; such neutral forms contain the NR structure, with its positive charge balanced by the presence of an adjacent negatively-charged ion. *Id.*; Ex. 28 at 80:11-18. By contrast, as Dr. Adams admitted during his deposition, the disclosed L-valine and L-phenylalanine esters of NR neither contain the NR structure nor are electrically neutral (unless

made into a salt). Ex. 28, 80:19-81:23, 91:8-92:6, 98:10-99:11. A POSA would thus not understand such NR esters to be NR, especially in the context of a claim to NR formulated for oral administration. *Id.*

b. Contrary to Elysium's Argument, NR Has a Defined Structure that Is Present in NR Salts But Not in Other Derivatives Such as Esters

Elysium argues that "there is no single 'defined structure' of nicotinamide riboside" because the "molecule can form two anomers (an α-anomer and a β-anomer) which have different structures." A POSA would understand, however, that the defined and recognized structure of NR, as shown below, includes any such anomers.

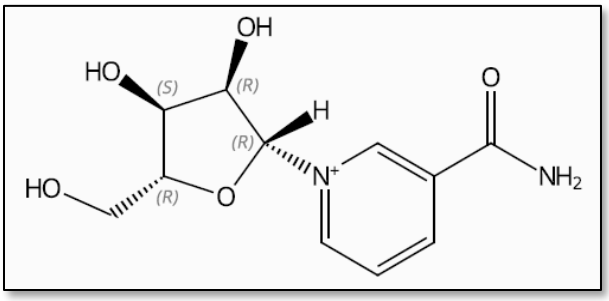


Ex. 29; *see* Ex. 28, 82:23-83:2; Ex. 12, ¶8 (conceding that the anomers "have identical chemical formulae"). A POSA would therefore understand that "nicotinamide riboside," as recited in the claims, refers to chemical compounds containing this defined structure.

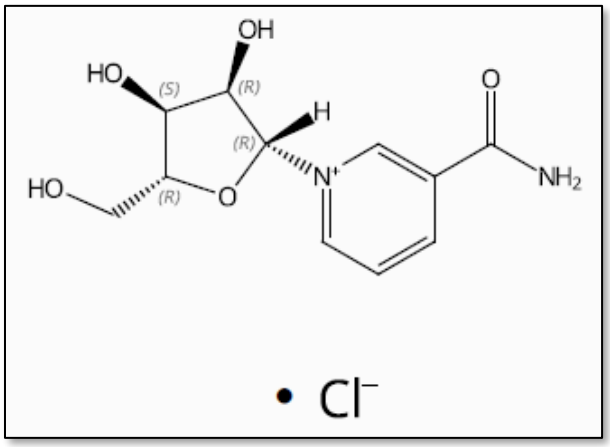
NR salts include the structure of NR, but NR esters do not. This fundamental difference between salts and esters results from their underlying structure: salts are

formed by the attraction between two oppositely charged ions (the positively charged NR and the negatively charged counterion), whereas esters are formed by covalently modifying the NR structure through a chemical reaction to create a covalent bond with an oxygen-containing molecule to form a new ester compound. Ex. 12 ¶15; Ex. 28, 84:4-86:15, 87:1-9, 90:15-19, 97:5-99:1.

Dr. Adams's testimony confirms that salts, but not esters, include the defined structure of NR. He testified that the following figures depict the NR molecule (left) and the NR Chloride salt (right):



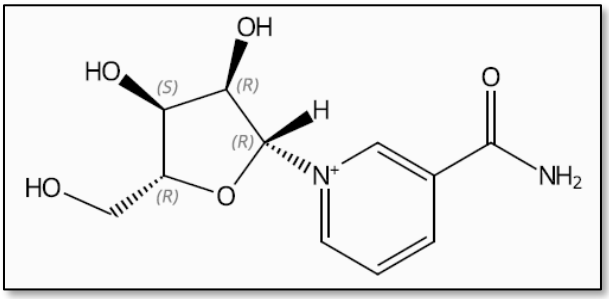
NR
Ex. 29



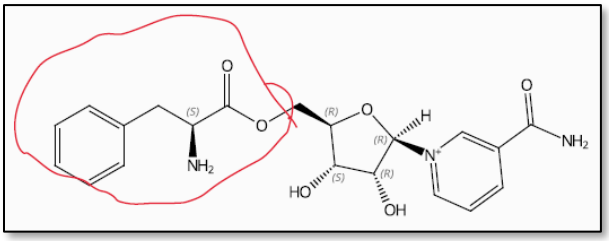
NR Chloride Salt
Ex. 30

Ex. 28, 84:4-85:15 (noting that, in the NR Chloride salt, the chloride molecule is joined to the NR molecule with an ionic bond), 86:3-15. As these figures show, the NR Chloride salt includes the defined structure of NR. *See also* Ex. 31 at ELY_0019944 (depicting the "Chemical Structure of NR" as the NR Chloride salt).

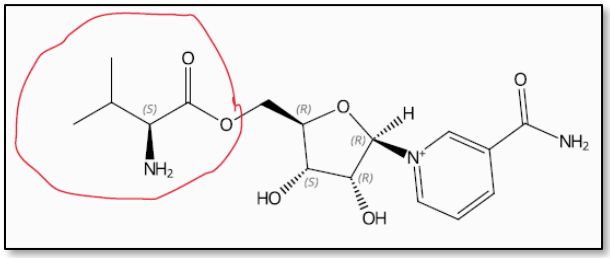
As Dr. Adams admitted during his deposition, however, the esters he identifies are structurally different from NR. As illustrated below, the structure of the NR molecule is not retained in NR esters because the esters substitute a completely different chemical structure for one of the "OH" groups that is found in NR, as Dr. Adams annotated during his deposition:



NR
Ex. 29



Phenylalanine Ester
Ex. 32



Valine Ester
Ex. 33

Ex. 28, 89:5-8, 90:20-91:7. Dr. Adams conceded that these changes make "the molecule very different" and will "have an enormous impact." *Id.*, 91:19-92:1, 97:5-99:1. Thus, a POSA would understand that "nicotinamide riboside" refers to NR base and NR salts, but not to NR derivatives such as esters that do not include the chemical structure of NR.

c. The Specification Does Not Define "Nicotinamide Riboside" to Include NR Esters

The statement that "the nicotinamide riboside *can be* a derivative (e.g. L-valine or L-phenylalanine esters) of nicotinamide riboside," '807 patent, 28:63-65, is not a definition of NR. Instead, it simply explains that in some embodiments the invention *can* encompass NR derivatives exemplified by the disclosed esters. Later in the paragraph, the specification confirms that "the present invention *also encompasses*" derivatives such as the disclosed esters. *Id.*, 29:4-8. These disclosures do not "clearly set forth a definition" of NR or "clearly express an intent" to redefine the term, and thus fall far short of the "exacting" standard for lexicography. *Thorner*, 669 F.3d at 1365-66. If anything, the statement that "the nicotinamide riboside *can be* a derivative (e.g. L-valine or L-phenylalanine esters) of nicotinamide riboside" shows that the inventor did not intend for esters to be part of the definition of "nicotinamide riboside" as recited in the claims.

When the inventor wanted to act as his own lexicographer, he used express definitional language. *See, e.g.*, '807 patent, 26:43-46 ("The term primer, as defined herein, is meant to encompass …"), *id.*, 20:16-20 ("As used herein, a nicotinamide riboside-related prodrug is …"). But the specification used no such express definitional language in disclosing that "the nicotinamide riboside *can be* a derivative (e.g. L-valine or L-phenylalanine esters) of nicotinamide riboside." *Id.*, 28:63-65.

In *Medicines Co. v. Mylan, Inc.*, 853 F.3d 1296 (Fed. Cir. 2017), the court held that when the specification uses express definitional language for certain terms but not for others, there is no lexicography for the latter. The patentees in *Medicines Co.* "use[d] a similar format" to define terms: "the defined term in quotation marks, followed by the terms 'refers to' or 'as defined herein.'" *Id.* at 1306. For the term "efficient mixing," however, the patentees did not use that definitional format, but instead simply stated what efficient mixing "is characterized by." *Id.* The court held that this statement "does not purport to be definitional because it does not accord with the linguistic formula used by the patentee to signal the designation of other defined terms," and it therefore "lacks the clear expression of intent necessary for a patentee to act as its own lexicographer." *Id.*

The file history of the related '832 application confirms that the inventor did not intend to define "nicotinamide riboside" to include derivatives that do not include the structure of NR. The examiner had remarked that "[t]he definition of the term 'nicotinamide riboside' provided in the specification encompasses derivatives of nicotinamide riboside," Ex. 34 at 4, but the applicant "disagree[d]" because "[a]lthough both isolated nicotinamide riboside as well as derivatives are described, these different types are simply alternatives that can be used in the method of the present invention." Ex. 35 at 5.

4. Elysium's Sur-Reply Position

Plaintiffs argue that "nicotinamide riboside" can include salts, but not other derivatives. Plaintiffs cannot have it both ways: either "nicotinamide riboside" excludes all derivatives or it must include any derivative, including those expressly recited in the specification.

The specification states:

> the nicotinamide riboside can be a derivative (e.g. L-valine or L-phenylalanine esters) of nicotinamide riboside.

'807 patent, 28:63-65. Plaintiffs seek to contradict the patent's definition of claim scope with unsupported attorney argument that a "POSA would understand that 'nicotinamide riboside' refers to NR base and NR salts." *Supra*, at 17.[8] Tellingly, they offer no expert testimony as to a POSA's understanding, basing their argument instead on a purported drawing of NR chloride salt, presented to Dr. Adams at his deposition. *See id.* at 16; Ex. 30. They ignore Dr. Adams' testimony that the drawing was "a very unusual way for a chemist to show a salt…. [N]ormally you show the… chloride link to the rest of the molecule through an ionic bond." Ex. 28 at 85. In NR chloride salt, the chloride is "bound to the nitrogen in the pyridine ring

[8] Plaintiffs' reliance on *Medicines Co. v. Mylan, Inc.*, 853 F.3d 1296, 1306 (Fed. Cir. 2017) is misplaced. The "most important" issue in *Medicines* was that the relied-upon portion of the specification "amounts to a mere recitation of the results obtained… rather than a definition of what the efficient mixing process is." *Id.* But, here, a description of what something can "be," defines the scope of what it is.

by an ionic bond." *Id.* Plaintiffs' drawing misleadingly omits this bond to imply that NR chloride is not a derivative.

Plaintiffs also assert, without expert support, that the esters recited in the specification could not be used "in the context of a claim to NR formulated for oral administration," pointing to Dr. Adams' testimony that these esters are not electrically neutral. *Supra*, at 14-15. Plaintiffs overlook that claim 1 of the '807 patent permits admixture of the composition with "saline." Dr. Adams testified that the esters would be stable under such conditions. Ex. 28 at 108 ("It's in water solution. When you put a positively-charged molecule into water, then it becomes stable"). Plaintiffs also disregard their own admission that "nicotinamide riboside" encompasses the NR base molecule, which itself is not electrically neutral. *Supra*, at 14.

Plaintiffs acknowledge that during prosecution of a related application, the examiner noted that "[t]he ***definition of the term 'nicotinamide riboside' provided in the specification*** encompasses derivatives of nicotinamide riboside." Ex. 34 at 4 (emphasis added). Clearly, the examiner viewed this language as definitional. In its response, Dartmouth acquiesced by amending the claim to exclude a composition "wherein the nicotinamide riboside is not a nicotinamide riboside derivative." Ex. 37 at 2.

B. "isolated nicotinamide riboside"

TERM (PATENT/CLAIMS)	CHROMADEX'S PROPOSED CONSTRUCTION	ELYSIUM'S PROPOSED CONSTRUCTION
"isolated nicotinamide riboside" '807 Patent: Claim 1	"nicotinamide riboside that is separated or substantially free from at least some of the other components associated with the source of the molecule such that the weight of the nicotinamide riboside is at least 25% of the total weight of the nicotinamide riboside and any other components associated with the source of the molecule in said composition"	"nicotinamide riboside that has been separated or is substantially free from at least some of the other molecules commonly associated with it"

1. ChromaDex's Opening Position

There are two "isolated" claim terms. Independent claim 1 of the '807 patent recites "[a] composition comprising *isolated nicotinamide riboside* …." Dependent claim 2 of both the '807 and '086 patents recites "[t]he composition [or 'pharmaceutical composition'] of claim 1, wherein *the nicotinamide riboside is isolated from a natural or synthetic source*." These terms are addressed in turn.

There are two disputes relating to the "isolated nicotinamide riboside" term. ***First***, does the isolated NR need to be separated or substantially free from at least some of "the other components associated with the source of the molecule"

(ChromaDex's position) or from at least some of "the other molecules commonly associated with it" (Elysium's position)? ***Second***, does isolated NR need to be at least 25% pure[9] (ChromaDex's position), or can NR be considered "isolated" even when nearly all of the other components associated with the source material remain in the composition, such that NR comprises an insignificant percentage of the total amount of source material in the composition (Elysium's position)? As discussed below, the Court should adopt ChromaDex's proposed construction because it is supported by the intrinsic (and extrinsic) evidence and is consistent with the construction adopted by the PTAB.

a. The Isolated NR Must Be Separated or Substantially Free from at Least Some of "the Other Components Associated with the Source of the Molecule"

The specification explains that "an isolated molecule" is one that is "separated or substantially free from at least some of the other components of the naturally occurring organism." '807 patent, 9:23-30.[10] Thus, the "isolated" NR recited in the claims must be separated or substantially free from at least some of the other components associated with the source of the molecule, whether that source is a

[9] This brief uses "purity" as a shorthand to refer to the weight of the NR as a percentage of the total weight of the NR and any other components associated with the source of the NR in a given composition.

[10] The '807 and '086 patents are related and share a common specification. For convenience, ChromaDex cites only the specification of the '807 patent, with the understanding that the '086 patent specification contains corresponding disclosures.

"naturally occurring organism," *id.*, or a "synthetic source" of NR, *id.*, cl. 2; '086 patent, cl. 2. The PTAB agreed, construing the term "is isolated" to mean "that the nicotinamide riboside is separated or substantially free from at least some of the other components associated with the source of the molecule such that it constitutes at least 25% (w/w) of the composition." Ex. 3 at 14. The Federal Circuit affirmed the PTAB's decision. *Elysium Health, Inc. v. Trustees of Dartmouth Coll.*, 796 F. App'x 745 (Fed. Cir. 2020).

Elysium proposes to construe "isolated nicotinamide riboside" to mean "nicotinamide riboside that has been separated or is substantially free from at least some of *the other molecules commonly associated with it*." This proposal, however, seeks to read into the claims what the specification expressly calls an "example." *See* '807 patent, 9:23-30. Moreover, there is no "clear indication in the intrinsic record that the patentee intended the claims to be" limited to that example, and thus "it is improper to read limitations from [that] embodiment … into the claims." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 913 (Fed. Cir. 2004).

Unlike ChromaDex's proposed construction, moreover, Elysium's proposed construction does not account for the disclosure that "an isolated molecule" is one that is separated or substantially free from at least some of the other components associated with the *source* of the molecule. *See* '807 patent, 9:23-30. Elysium proposes that the NR must be separated or substantially free from "at least some of

the other molecules commonly associated with it," but "the other molecules commonly associated with" NR are not necessarily the same as the other components associated with the source of the NR, as disclosed in the specification.

b. The Claimed Isolated Nicotinamide Riboside Must Be at Least 25% Pure

ChromaDex proposes that the term "isolated nicotinamide riboside" requires at least 25% purity, whereas Elysium's proposal "would encompass separation of even an insignificant amount of other components." Ex. 3 at 13. Elysium's position here is a rehash of its failed argument in the IPR that the challenged claims were anticipated, for example, by skim milk—because fat had been skimmed from the milk—despite the fact that "significant amounts of other components remain [in the skim milk] after the fat is removed" and that the skim milk contains only insignificant amounts of NR. *Id.* at 26-27. The PTAB correctly found that Elysium's position "would render the term[s] unreasonably broad" and that the specification "counsel[s] against such a broad construction." *Id.* at 13. Notably, the Board applied the "broadest reasonable construction" standard. Ex. 3 at 5-6. Since Elysium's proposed construction is "unreasonably broad" even under the broadest reasonable construction, *id.* at 13, it is even more unreasonable under the narrower claim construction standard articulated in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc), and applied by this Court.

In contrast to Elysium's overbroad proposed construction, ChromaDex's proposed construction is supported by the specification. As the PTAB found, "the Specification provides guidance as to how pure a molecule need[s] to be to be deemed 'isolated.'" Ex. 3 at 12. Specifically, it teaches that "[w]hen the isolated molecule is a polypeptide, said polypeptide is at least about 25%, 50%, 60%, 70%, 75%, 80%, 85%, 90%. 95%, 97%, 98%, 99% or more pure (w/w)." '807 patent, 9:30-32. Although the specification references 25% purity with regard to polypeptides, the PTAB found "no reason why [a POSA] would have viewed the term 'isolated' differently for nucleic acids than for polypeptides." Ex. 3 at 14; *see* Ex. 2 at 7. Thus, the term "isolated nicotinamide riboside" should be construed to require the NR to be separated or substantially free from at least some of the other components associated with the source of the molecule such that the weight of the nicotinamide riboside is at least 25% of the total weight of the nicotinamide riboside and any other components associated with the source of the molecule in said composition.

2. Elysium's Answering Position

a. Elysium's Construction Adopts the Specification's Express Definition of "Isolated Molecule"

Elysium's construction of "isolated nicotinamide riboside" applies the specification's express definition of "isolated molecule." It states:

> As used herein, an isolated molecule… ***means*** a molecule separated or substantially free from at least some of the other components of the naturally occurring organism, such as for example, the cell structural components or other polypeptides or nucleic acids commonly found associated with the molecule.

'807 patent at 9:23-31 (emphasis added). Elysium's construction of "isolated nicotinamide riboside" as "nicotinamide riboside that has been separated or is substantially free from at least some of the other molecules commonly associated with it" tracks the patent's definition.[11]

Plaintiffs' argument that the specification's definition is merely an "example" is wrong. *Supra*, at 24. The specification explains that this is what the patent "***means***" by "isolated." The word "means" connotes a definition, not an example. There can be no doubt that the patentee chose to create its own definition here.

b. There is no Support for a 25% Purity Requirement

Plaintiffs' engrafting of a 25% purity requirement onto a definition that does not purport to dictate a required level of purity lacks support in logic or patent law. Plaintiffs rely chiefly on the subsequent sentence in column 9 that adds a purity level requirement for isolated molecules that are polypeptides, stating that "***[w]hen the isolated molecule is a polypeptide***, ***said polypeptide*** is at least about 25%, 50%,

[11] Construction is necessary, for example, because Plaintiffs seek to avoid prior art references describing NR that has been separated from molecules associated with the NR but which do not report the specific level of purity obtained.

60%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98%, 99% or more pure (w/w)." '807 patent at 9:30-32 (emphasis added). It is undisputed that nicotinamide riboside is not a polypeptide. Thus, that sentence cannot define isolated NR. If the patentee meant to define ***all*** "isolated molecules" as subject to a purity requirement, it would not have begun the sentence with the phrase "[w]hen the isolated molecule is a polypeptide…." Notably, Plaintiffs point to no statement elsewhere in the specification imposing a level of purity requirement on an isolated nucleic acid, vitamin, or any other isolated molecule that is not a polypeptide.

In asserting that the purity requirement for polypeptides applies to all other isolated molecules, Plaintiffs cite the PTAB's bald statement that there is "no reason" a POSA "would have viewed the term 'isolated' differently for nucleic acids than for polypeptides. *Supra,* at 26 (quoting Ex. 3 at 14). With due respect, NR is not a nucleic acid, and the PTAB's statement was not supported by any intrinsic or extrinsic evidence (nor is Plaintiffs' argument). Indeed, contrary to Plaintiffs' argument, the juxtaposition of the two sentences in column 9 shows that the patentee viewed polypeptides as different from other molecules. Nucleic acids, for example, play an entirely different role in the patent's disclosed embodiments, such as their use in an expression vector to encode an NR kinase. *E.g.* '807 patent: 3:36-38. In all, the term "isolated nucleic acid" appears no fewer than 24 times in the

specification, yet at no time did the patentee associate any particular purity level with that term.

Plaintiffs argue that the polypeptide sentence exemplifies an "isolated molecule" and provides "guidance" as to how pure an isolated molecule must be. This argument defies the rules of English grammar. The sentence defines a subset of "isolated molecules" limited to polypeptides; it has no effect on the meaning of "isolated" for molecules that are not polypeptides.

Ironically, Plaintiffs elsewhere acknowledge that, without a "clear indication in the intrinsic record that the patentee intended the claims to be limited to [an] example… it is improper to read limitations from that embodiment into the claims." *See supra*, at 24. But Plaintiffs are guilty of exactly that error in insisting that the Court impose a 25% purity requirement on all isolated molecules just because there is a specific purity requirement applicable to isolated polypeptides.

The Federal Circuit's decision in *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363 (Fed. Cir. 2009), overturning a district court's claim construction, is on point. In *Martek*, the specification defined "animal" to mean "any organism belonging to the kingdom Animalia." *Id.* at 1380. The district court construed the claim to include only non-human animals, based on an exemplary sentence following the definition that "[p]referred animals from which to produce a food product include any economic food animal." *See id.* at 1380-81. The defendant

successfully argued to the district court that this evidenced an intent to limit "animal" to non-human animals notwithstanding the broader express definition of that term. *Id.* at 1380.

The Federal Circuit reversed, holding that where a patentee has defined a claim term in the specification, "[t]hat definition controls." *Id.* The court explained that it was improper to use narrower examples to limit an express, broader, definition of a claim term. This is because where "the patentee has used no words or expressions that manifestly exclude coverage of humans… it would be improper to override the patentee's express definition of 'animal' to limit the scope of the claims…. [A]bsent a clear intention to restrict the invention to particular members of the kingdom Animalia, we cannot limit the claims to the listed preferred embodiments." *Id.* at 1381.

Here, Plaintiffs invite the same error. They ask this Court to limit the definition of "isolated" to require 25% purity for all molecules simply because the specification requires 25% purity for polypeptides. But that falls far short of *Martek*'s standard, which would require "words or expressions that manifestly exclude coverage of" non-polypeptide molecules that are less than 25% pure. *See id.* at 1381. Indeed, the language of the specification connotes the opposite, imposing the 25% purity requirement only "when" the isolated molecule is a

polypeptide. This means that the 25% purity requirement does not apply more generally to all isolated molecules.

There is another flaw in Plaintiffs' argument. They define "purity" as "the weight of the NR as a percentage of the total weight of the NR and any other components associated with the source of the molecule in said composition." *Supra*, at 22; *see also id.* at 23 n.9. This definition is generated entirely out of whole cloth. In chemistry, the purity of a composition would be calculated as weight over weight ("w/w"), a simple calculation that would compare the total weight of NR in the composition to the total weight of the composition as a whole.[12] *See* Ex. 26. Plaintiffs offer no expert opinion, nor do they reference any part of the specification, to support their unconventional and confusing measurement of the weight of components "associated with the source of the molecule."

Plaintiffs' construction would also render the claims indefinite. There is no teaching in the patent, and no understanding of a POSA, as to which specific components in the composition should be deemed "associated with the source of the [NR]" and which should not. This is further reason not to adopt it.

[12] As discussed below, the PTAB recited a "w/w" calculation when it imposed its 25% purity limitation. Ex. 3 at 12. Thus, while Plaintiffs rely heavily on the PTAB's construction, they propose an entirely different calculation of the level of purity.

c. The Court is not Bound by the PTAB's Construction of "Isolated"

The Court is not bound by the PTAB's construction of "isolated" as imposing a 25% purity requirement. Plaintiffs implicitly acknowledge this: as noted, although they cite the PTAB's construction with approval they do not themselves adopt it, because it was based on "w/w of the composition." Ex. 3 at 14. By contrast, Plaintiffs, as discussed above, would have the Court impose an entirely different percentage purity requirement. Under their construction, purity would be measured not as w/w, but by comparing the weight of the NR in the composition to the weight of the NR plus "any other components associated with the source of the molecule in the composition." *Supra*, at 22.

In fact, neither the parties nor the Court are bound by the PTAB's construction. On appeal, the Federal Circuit issued a summary affirmance of the PTAB's judgment, ruling that claim 2 of the '086 patent is not invalid as anticipated. Ex. 27. However, "[a] Rule 36 [summary affirmance] judgment simply confirms that the trial court entered the correct judgment. It does not endorse or reject any specific part of the trial court's reasoning." *TecSec, Inc. v. IBM*, 731 F.3d 1336, 1343 (Fed. Cir. 2013). Moreover, where a "summary disposition affirms a decision that rested on multiple grounds, the affirmance is generally not binding precedent for either ground." *Id.*

Here, as in *TecSec*, the PTAB's decision rested on multiple grounds.[13] Indeed, during arguments before the Federal Circuit, Dartmouth's counsel was asked "[i]f we conclude that the PTAB's claim construction is not supportable because they incorporated the 25 percent from an inappropriate part of the written description, can we still find that they were correct in their anticipation ruling?" Ex. 19 at 22. Dartmouth's counsel's answer: "Absolutely…" He argued that affirmance was appropriate "regardless of the claim construction" and that "[y]ou don't need a construction of isolated in order to affirm the Board's decision." *Id.* at 22-24. *See United Access Techs., LLC v. Centurytel Broadband Servs., LLC*, 2016 U.S. Dist. LEXIS 135455, at *13 (D. Del. Sep. 30, 2016) (collateral estoppel did not apply to summary affirmance where party made "express appellate argument for affirmance on alternative, independent grounds"). This Court's claim construction must be based on the teachings of *Phillips*, not on any reliance on the PTAB's decision.

3. ChromaDex's Reply Position

As demonstrated in ChromaDex's opening brief, the recited "isolated nicotinamide riboside" must be separated or substantially free from at least some of "the other components associated with the source of the molecule" and must be at least 25% pure. Elysium has failed to show otherwise.

[13] The PTAB expressly applied two alternative constructions of "isolated" to claim 2. Ex. 3 at 26-27.

a. Elysium's Proposal that the Recited Isolated NR Must Be Separated or Substantially Free from at Least Some of "the Other Molecules Commonly Associated with It" Is Inconsistent with the Specification

Elysium argues that its proposed construction "tracks the patent's definition," but the specification's plain language shows otherwise. The specification states that "an isolated molecule" is one that is "separated or substantially free from at least some of the other components of the naturally occurring organism." '807 patent, 9:23-30.[14] It then explains that "example[s]" of "the other components of the naturally occurring organism" are the components "commonly found associated with" the NR. *Id.* Elysium's proposed construction incorporates this "example"—requiring that the isolated NR be separated or substantially free from at least some of the other molecules "commonly associated with" the NR—which is improper because there is no "clear indication in the intrinsic record that the patentee intended the claims to be" so limited. *Liebel-Flarsheim*, 358 F.3d at 913.

b. The 25% Purity Requirement Applies to the Claimed Isolated NR, and Elysium Cannot Show Otherwise

Reprising its failed arguments from the IPRs, Elysium argues that the specification's statement that "an isolated molecule" is one that is "separated or

[14] ChromaDex's proposed construction tracks this disclosure, requiring that the NR "is separated or substantially free from at least some of the other components associated with the source of the molecule," whether that source is "a natural or synthetic source" of NR. '807 patent, cl. 2; '086 patent, cl. 2.

substantially free from at least some of the other components" of the source of the molecule, '807 patent, 9:23-30, "does not purport to dictate a required level of purity." As the PTAB recognized, however, that disclosure must be read to require some minimum level of purity because, even applying "the broadest reasonable interpretation standard," it "would be unreasonable … to construe 'isolated' to only require separation from 'some'—no matter how insignificant—amount of other components of the natural source of nicotinamide riboside (e.g., cow's milk)." Ex. 2 at 7-8; Ex. 3 at 13.

The specification "provides guidance concerning the required purity of an 'isolated molecule'" by disclosing that "[w]hen the isolated molecule is a polypeptide, said polypeptide is at least about 25%, 50%, 60%, 70%, 75%, 80%, 85%, 90%. 95%, 97%, 98%, 99% or more pure (w/w)." '807 patent, 9:30-32; Ex. 2 at 7; Ex. 3 at 12. Although the specification references 25% purity with regard to polypeptides, the PTAB found "no reason why [a POSA] would have viewed the term 'isolated' differently for nucleic acids than for polypeptides." Ex. 3 at 14; *see* Ex. 2 at 7.

Elysium argues that "nicotinamide riboside is not a polypeptide" and therefore that the disclosed 25% purity requirement "cannot define isolated NR" as a matter of "grammar." But in its rigid focus on the specification's grammar, Elysium misses the essence of the PTAB's reasoning, which focused on how a POSA would

understand the specification. Although the PTAB recognized that the specification does not *expressly* impose a 25% purity requirement on isolated molecules other than polypeptides, it found that the *only reasonable reading* of the specification is that the isolated molecule must have some minimum level of purity. And the PTAB found "guidance" regarding that minimum level of purity in the disclosure that an isolated polypeptide must be at least 25% pure. Ex. 2 at 7; Ex. 3 at 12.

Elysium cites *Martek Biosciences* for the proposition that the 25% purity requirement is merely an embodiment and should not be read into the claims. But *Martek* is inapposite. It held that the term "animal" was not limited to non-human animals because the specification broadly defined "animal" to mean "any organism belonging to the kingdom Animalia," and because there was no basis for limiting that definition to the embodiments of non-human animals. 579 F.3d at 1380-81. Here, by contrast, the 25% purity requirement does not merely describe one example of a broader disclosed category. Instead, the 25% purity requirement provides guidance regarding the *meaning* of the description of an isolated molecule as "separated or substantially free from at least some of the other components" of the source of the molecule. '807 patent, 9:23-30.

Finally, Elysium criticizes ChromaDex's proposed requirement that "the weight of the nicotinamide riboside is at least 25% of the total weight of the nicotinamide riboside and any other components associated with the source of the

molecule in said composition," asserting that any purity requirement should be "calculated as weight over weight ('w/w')," which "would compare the total weight of NR in the composition to the total weight of the composition as a whole."

Elysium's criticisms miss the mark. The purpose of the 25% purity requirement is to measure the degree to which the isolated NR is "separated or substantially free from at least some of the other components" of the source of the NR. *Id.*, 9:23-32. The appropriate calculation, therefore, is not the total weight of NR relative to the total weight of the composition for oral administration (e.g., a tablet), but instead the total weight of NR relative to the total weight of the components associated with the source of the NR in the composition (e.g., the components of the isolation product resulting from isolating NR from a synthetic source).[15]

4. Elysium's Sur-Reply Position

The specification provides an express definition: "[a]s used herein, an isolated molecule… ***means***…." '807 patent, 9:23-25. This is the very language that

[15] Elysium notes that the 25% purity requirement in the PTAB's construction measured the total weight of the NR relative to the total weight of the "composition." But that was because the "compositions" at issue in the IPRs—skim milk and buttermilk—*were* the alleged isolation product, resulting from allegedly isolating the NR from whole milk by removing fat. By contrast, the compositions at issue here—dietary supplements such as capsules—comprise the isolation product together with other components (e.g., carriers).

Plaintiffs elsewhere concede is "express definitional language." *Supra*, at 18. The definition requires only that an "isolated" molecule be "separated or substantially free from at least some of the other components" commonly found associated with the naturally-occurring molecule. '807 patent, 9:23-31.

As justification for supplanting this definition, Plaintiffs rely on the PTAB's statement that the definition is "unreasonable" because it does not specify a minimum purity requirement. *Supra*, at 35. But the PTAB was not at liberty to add additional requirements to an express definition to make it more "reasonable." For example, in *In re Bass*, the specification defined the term "motorized sports boat" as a boat meeting only two requirements: a cabin and a certain length. 314 F.3d 575, 577 (Fed. Cir. 2002). The claim was invalidated over a prior art fishing boat that met those two requirements. The patentee argued that "sports boat" could not reasonably be construed to include a boat with a fishing hold. The Federal Circuit disagreed, explaining that the PTO must "tak[e] into account any definitions presented in the specification." *Id.* It explained that the patentee "chose to define 'motorized sports boat' in the specification" by way of only two requirements and "cannot change or modify that definition on appeal." *Id.*

Here, Plaintiffs admit that the specification "does not expressly impose a 25% purity requirement on isolated molecules other than polypeptides…." *Supra*, at 36. It is undisputed that NR is not a polypeptide. Plaintiffs offer no evidentiary support

for their attorney argument that the polypeptide purity requirement was meant to provide "guidance" covering all "isolated molecules." This is made up out of whole cloth.

Plaintiffs also do not explain why it is unreasonable to construe "isolated" as broadly as the applicant defined it in the specification. Indeed, in claim 1 of the '086 patent, the applicant omitted the "isolated" limitation altogether, giving that claim even broader scope. Moreover, in Dartmouth's preliminary response to Elysium's IPR petition, Dartmouth's proposed claim construction did not include ***any*** purity requirement for "isolated nicotinamide riboside." Ex. 5 at 7. Instead, Dartmouth proposed that the term be construed to mean "nicotinamide riboside that is substantially free from other molecules." *Id.* Dartmouth described its proposed construction as "the way a person of ordinary skill in the art would understand ['isolated']" in view of the specification's definition. *Id.* at 8. Dartmouth never suggested that "isolated" imposed a purity requirement until the PTAB, *sua sponte*, provided a construction that worked to Dartmouth's advantage in distinguishing Elysium's prior art.

Plaintiffs' reliance on the PTAB's construction must be rejected for another reason: the 25% purity requirement Plaintiffs now espouse is not the same 25% purity requirement that the PTAB imposed. Plaintiffs cannot cite the PTAB as

authority for their proposed claim construction while at the same time rejecting the PTAB's actual construction.

Plaintiffs do not deny that the PTAB's purity requirement was that NR constitute "25% (w/w) ***of the composition***." Ex. 2 at 8 (emphasis added). Plaintiffs endorsed the PTAB's calculation in the IPR proceedings, *see* Ex. 6 at 18-19, but now propose an entirely different calculation: the NR must be "25% of the total weight of the [NR] and any other components associated with the source of" the NR. Their latest construction is litigation-inspired. Nowhere in the specification is such a calculation disclosed.[16] Plaintiffs' shifting explanation of their proposed purity requirement only underscores its lack of any sound mooring in the specification.

[16] Plaintiffs' proposal would also render the claim indefinite. How would anyone reading the claim know which components in a composition are "associated with" the source of NR?

C. "the nicotinamide riboside is isolated from a natural or synthetic source"

TERM (PATENT/CLAIMS)	CHROMADEX'S PROPOSED CONSTRUCTION	ELYSIUM'S PROPOSED CONSTRUCTION
"the nicotinamide riboside is isolated from a natural or synthetic source" '807 Patent: Claim 2 '086 Patent: Claim 2	"nicotinamide riboside that is separated from at least some of the other components associated with the source of the molecule such that the weight of the nicotinamide riboside is at least 25% of the total weight of the nicotinamide riboside and any other components associated with the source of the molecule in said composition"	"the nicotinamide riboside is obtained from a natural source such as milk or a synthetic source such as a chemical library and is not chemically synthesized"

1. ChromaDex's Opening Position

Claim 2 of the '807 patent and claim 2 of the '086 patent are dependent claims that recite that "the nicotinamide riboside *is isolated from a natural or synthetic source*." As explained below, "is isolated from a natural or synthetic source" should be construed as "*is separated from* at least some of the other components associated with the source of the molecule such that the weight of the nicotinamide riboside is at least 25% of the total weight of the nicotinamide riboside and any other components associated with the source of the molecule in said composition."

Elysium's proposed construction, which is inconsistent with the claim language and relies on a baseless disclaimer argument, should be rejected.

a. "Is Isolated from" Means the NR "Is Separated from" Other Components

As discussed above, "isolated NR" as recited in claim 1 of the '807 patent should be construed to mean "nicotinamide riboside *that is separated or substantially free from* at least some of the other components associated with the source of the molecule such that" the NR is at least 25% pure. The claim term "is isolated from a natural or synthetic source," as recited in dependent claim 2 of the '807 patent and of the '086 patent, should be construed similarly but more narrowly to require that the NR "is separated from" at least some of the other components associated with the source of the NR instead of the NR being "separated *or* substantially free from" those other components.

Under the doctrine of claim differentiation, dependent claim 2 of the '807 patent should be construed more narrowly than independent claim 1.[17] *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1242 (Fed. Cir. 2003). ChromaDex's proposed constructions account for claim differentiation. For independent claim 1,

[17] Although claim 2 of the '086 patent does not depend from an independent claim that recites an "isolated" term, it is undisputed that the term "is isolated from a natural or synthetic source" has the same meaning in claim 2 of the '807 patent and claim 2 of the '086 patent.

ChromaDex proposes that the term "isolated nicotinamide riboside" requires that the NR is *either* "separated" *or* "substantially free" from at least some of the other components associated with its source. For dependent claim 2, ChromaDex proposes a narrower construction for the term "is isolated *from* a natural or synthetic source"—consistent with the claim language—to require that the NR "is separated from" at least some of the other components associated with its source.

b. Elysium's Proposed Construction Is Inconsistent with the Language of Claim 2

Elysium proposes to construe the term "the nicotinamide riboside is isolated from a natural or synthetic source" to mean "the nicotinamide riboside is obtained from a natural source such as milk or a synthetic source such as a chemical library and is not chemically synthesized." But this proposed construction departs from the claim language. Claim 2 recites that the NR "is isolated from" a natural or synthetic source, and that has a different meaning from NR that "is obtained from" a natural or synthetic source, as proposed by Elysium. Furthermore, there is no basis for Elysium's attempt to import into claim 2 the requirement that the NR "is not chemically synthesized." That requirement does not explain how the NR "is isolated from a natural or synthetic source," as recited in claim 2. Instead, it limits how the "natural or synthetic source" of NR is created, even though nothing in the language of claim 2 limits how the source of NR is created.

Essentially, Elysium is attempting to conflate the creation of the claimed "natural or synthetic source" of NR with the "isolat[ion]" of NR "from" that source. But a POSA would understand that these are separate, as illustrated by Elysium's own patent application. That application discloses using chemical synthesis to *create* an intermediate product from which NR can be isolated (*i.e.*, a *synthetic source* of NR) followed by steps to *isolate* NR from that *synthetic source* (where it would be present, for example, along with reactants and reaction by-products). Ex. 4. Specifically, Example 4 discloses that chemical synthesis was performed to *create a synthetic source* of NR,[18] and that NR was subsequently "*isolated* via filtration." *Id.* at 41-42. Similarly, Example 6 discloses that chemical synthesis was performed to *create a synthetic source* of NR, followed by "*[i]solation* of nicotinamide riboside chloride (NR-B)" from that *synthetic source*. *Id.* at 43-44.

c. Dartmouth Did Not Disclaim Nicotinamide Riboside that Results from Chemical Synthesis from the Scope of Claim 2

Lacking any basis in the language of claim 2, Elysium's proposed construction relies on a contrived argument—made in the hopes of avoiding infringement—that Dartmouth disclaimed from the scope of claim 2 any NR that

[18] The application refers to NR as "Compound 4." *See* Ex. 4 at 17.

results from chemical synthesis.[19] As discussed below, however, there was no disclaimer, either in the specification or the prosecution history.

i. There Was No Specification Disclaimer

To establish specification disclaimer, Elysium must show that the inventor "demonstrate[d] an intent to deviate from the ordinary and accustomed meaning of a claim term by including in the specification expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." *Epistar Corp. v. Int'l Trade Comm'n*, 566 F.3d 1321, 1334 (Fed. Cir. 2009) (internal quotation marks omitted).

Elysium cannot meet its burden because the specification does not clearly and unmistakably disclaim NR that results from chemical synthesis from the scope of claim 2. The specification explains that "[t]he source of nicotinamide riboside can be from a natural or synthetic source identified by the method of the instant invention, or can be chemically synthesized." '807 patent, 28:58-63. Nothing in this disclosure suggests that a "synthetic source" of NR cannot be the product of a chemical synthesis. And for good reason: a compound produced by a synthetic reaction, from which NR can be isolated, is, by definition, a "synthetic source" of NR. The NR that is subsequently *isolated* from the result of that synthetic reaction

[19] Elysium advised ChromaDex of this argument in an April 27, 2020, letter after ChromaDex served its infringement contentions.

would be both "chemically synthesized" and "isolated from a natural or synthetic source."

ii. There Was No Prosecution History Disclaimer

Prosecution history disclaimer "preclud[es] patentees from recapturing through claim interpretation specific meanings disclaimed during prosecution." *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1359 (Fed. Cir. 2017) (internal quotation mark omitted). "[T]he alleged disavowing actions or statements made during prosecution [must] be both clear and unmistakable," *id.* (internal quotation mark omitted)—"both so clear as to show reasonable clarity and deliberateness and so unmistakable as to be unambiguous evidence of disclaimer," *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1325 (Fed. Cir. 2003) (citations omitted). The Federal Circuit has "consistently rejected prosecution statements too vague or ambiguous to qualify as a disavowal of claim scope," *Omega Eng'g*, 334 F.3d at 1325, including where the prosecution statements are simply "amenable to multiple reasonable interpretations," *Avid Tech., Inc. v. Harmonic, Inc.*, 812 F.3d 1040, 1045 (Fed. Cir. 2016). "The party seeking to invoke prosecution history disclaimer bears the burden of proving the existence of a 'clear and unmistakable' disclaimer," *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1063-64 (Fed. Cir. 2016), and must "overcome a heavy presumption that claim terms carry their full ordinary and customary meaning." *Epistar Corp.*, 566 F.3d at 1334.

Elysium cannot show a clear and unmistakable disclaimer. In the IPRs, citing the specification disclosure discussed above, Dartmouth stated that "Claim 2 is narrower than claim 1 because it further specifies that the nicotinamide riboside 'is isolated from a natural or synthetic source,' to the exclusion of chemically synthesizing the compound." Ex. 5 at 13 (citing '807 patent, 28:58-63). This statement did not clearly and unmistakably disclaim *synthetic sources* of NR that result from *chemical synthesis*. As discussed above, a compound produced in a synthetic reaction, from which the compound can be isolated, is, by definition, a "synthetic source" of the compound. Thus, the plain language used in the specification and in Dartmouth's statements in the IPRs belies any argument that Dartmouth disclaimed NR that is isolated from the reactants of a chemical synthesis.

Dartmouth's statement is more naturally read to mean that claim 2 excludes NR that is chemically synthesized but not "isolated from a natural or synthetic source." This interpretation makes sense in light of the dispute in the IPRs. Elysium argued that claim 2 is anticipated by alleged prior art references that disclose skim milk and buttermilk. Dartmouth responded that these references do not anticipate claim 2 because they do "not disclose any separation or extraction of individual components from the milk," and thus do "not disclose the claimed nicotinamide riboside 'that is isolated from a natural or synthetic source.'" *Id.* at 27, 36.

Since the NR in the alleged prior art milk was not chemically synthesized, Dartmouth's statement that claim 2 requires that the NR "'is isolated from a natural or synthetic source,' to the exclusion of chemically synthesizing the compound," *id.* at 13, was not "deliberately" aimed at excluding any NR that is the product of chemical synthesis. *See Omega Eng'g*, 334 F.3d at 1325. Instead, in the context of the dispute in the IPRs, Dartmouth's statement meant that claim 2 requires the NR to be "separat[ed] or extract[ed]" from at least some of the other components associated with the source of the molecule, in contrast to NR that is chemically synthesized without any separation or extraction step (for example, where the NR is used along with the other reaction products).

Even assuming for the sake of argument that Dartmouth's statements in the IPRs were otherwise a "clear and unmistakable" disclaimer of NR that results from chemical synthesis from the scope of claim 2, they would not give rise to prosecution history disclaimer because the PTAB rejected Dartmouth's proposed claim construction and Dartmouth acquiesced in the PTAB's rejection. In *Ecolab, Inc. v. FMC Corp.*, 569 F.3d 1335 (Fed. Cir.), *amended on reh'g in part*, 366 F. App'x 154 (Fed. Cir. 2009), the Federal Circuit held that a patentee's statements during prosecution were "not clear and unmistakable enough to invoke the doctrine of prosecution history disclaimer" where "a reasonable reader of this prosecution history could conclude" that the patentee's statements 'were hyperbolic or

erroneous, that the Examiner corrected [the patentee]'s error in the following communication, that [the patentee] recognized its error and never again repeated or relied upon the erroneous rationale, and that the claims were allowed for reasons independent of the allegedly disclaiming statements." *Id.* at 1343; *see Zoho Corp. v. Sentius Int'l, LLC*, C.A. No. 19-1 (YGR), 2020 WL 3128910, at *12 (N.D. Cal. June 12, 2020) ("the patentee's non-renewal of the [rejected] argument may indicate recognition of the error and acquiescence to the examiner's view").[20]

The acquiescence discussed in *Ecolab* is present here. In the -1795 IPR, challenging the '086 Patent, Dartmouth made the allegedly disclaiming statements in its Preliminary Response in support of its proposed construction of the term "is isolated from a natural or synthetic source" as recited in claim 2. The PTAB rejected Dartmouth's proposed claim construction in its Institution Decision. In its Patent Owner Response, Dartmouth summarized its claim construction arguments from its Preliminary Response, but did not ask the Board to adopt its previously proposed construction and instead "acquiesce[d] to the [Board]'s" construction of "is isolated." Ex. 6 at 17-19; *Zoho*, 2020 WL 3128910, at *12; *see Ecolab*, 569 F.3d at

[20] Similarly, the Federal Circuit recently held that, "[w]hile clear and limiting statements made by the patent owner can give rise to disclaimer, they do not in this case where those statements were clearly and expressly rejected by the Patent Office." *Galderma Labs., L.P. v. Amneal Pharm. LLC*, 806 F. App'x 1007, 1010-11 (Fed. Cir. 2020).

1343. For example, in distinguishing the asserted prior art, Dartmouth applied the PTAB's construction of "is isolated," not the construction it had previously proposed. *Id.* at 31. Finally, the Board's conclusions in its Final Written Decision were based on "reasons independent of the allegedly disclaiming statements." *Ecolab*, 569 F.3d at 1343. Thus, prosecution history disclaimer does not apply.[21]

iii. Extrinsic Evidence Confirms that a POSA Would Not Understand Dartmouth to Have Disclaimed "Synthetic Sources" of NR That Are the Product of Chemical Synthesis

As discussed above, Elysium's own patent application shows that a POSA would understand that the creation of the claimed "natural or synthetic source" of NR is distinct from the "isolat[ion]" of NR "from" that source. As the specification and claims of the Asserted Patents contemplate, Elysium's patent application describes processes in which synthetic reactions *create a synthetic source* of NR, and subsequent steps *isolate* NR from that *synthetic source*. Ex. 4.

[21] In the -1796 IPR, challenging the '807 patent, the PTAB denied institution, and thus Dartmouth could not respond to the Board's claim constructions. Nonetheless, Dartmouth's acquiescence to the Board's claim constructions in the -1795 IPR, challenging the '086 patent, defeats any prosecution history disclaimer based on Dartmouth's statements in the -1796 IPR, challenging the '807 patent, because the '086 patent is a continuation of the '807 patent, and claim 2 of both patents recites the same "is isolated" term. *See Ormco Corp. v. Align Tech., Inc.*, 498 F.3d 1307, 1314 (Fed. Cir. 2007); *Baxter Healthcare Corp. v. Mylan Labs. Ltd.*, 346 F. Supp. 3d 643, 659 (D.N.J. 2016).

Both ChromaDex and Elysium [redacted]. *See* Ex. 7 at CDXDE_000002257–CDXDE_000002258 ([redacted]); Ex. 8 at ELY_0077603-ELY_0077604 ([redacted]); Ex. 9 ([redacted]). The parties' respective manufacturing processes inform the claim construction analysis. *See Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322, 1326–27 (Fed. Cir. 2006) ("knowledge of [an accused] product or process provides meaningful context for the first step of the infringement analysis, claim construction").

This extrinsic evidence shows that a POSA would understand that the specification and Dartmouth's statements in the IPRs both contemplate processes in which chemical synthesis *creates* the *synthetic source* of NR, and subsequent steps *isolate* the NR from that *synthetic source*. A POSA would understand, that is, that the specification and Dartmouth's statements in the IPRs allow NR to be *both*

chemically synthesized *and* isolated from a synthetic source. This extrinsic evidence therefore confirms that Dartmouth did not clearly and unmistakably disclaim NR that is the product of chemical synthesis from the scope of claim 2.

2. Elysium's Answering Position

Claim 2 of the Asserted Patents, which each depends from claim 1, includes an additional limitation that the "nicotinamide riboside is isolated from a natural or synthetic source." This requirement adds a source limitation to the dependent claims. For example, claim 1 of the '807 specifies combining "isolated nicotinamide riboside" with any of three NAD+ precursors, whereas claim 2 more narrowly specifies that the isolated nicotinamide riboside must come from "a natural or synthetic source." The specification describes three distinct sources of NR: (1) natural sources, such as cow's milk; (2) synthetic sources, such as commercially available chemical libraries; and (3) chemically-synthesized NR. '807 patent at 27:39-54; 28:58-63. Claim 1 embraces all three sources of NR, while dependent claim 2, by omission, excludes chemically-synthesized NR.

The specification and other intrinsic evidence, including Dartmouth's admissions in the IPR proceedings, establish that this phrase should be construed as

"the nicotinamide riboside is obtained from a natural source such as milk or a synthetic source such as a chemical library and is not chemically synthesized."[22]

a. The Specification Distinguishes Obtaining NR "From a Natural or Synthetic Source" from Chemically Synthesized NR

"Isolated from a natural or synthetic source" in dependent claim 2 must specify "a further limitation of the subject matter claimed...." *See* 35 U.S.C. § 112 (pre-AIA). As Judge Andrews has explained, "[a] dependent claim that does not properly narrow the scope of the claim from which it depended is invalid under 35 U.S.C. § 112, ¶ 4." *Amgen Inc. v. Hospira, Inc.*, 2016 U.S. Dist. LEXIS 164744, * 9 (D. Del. Nov. 30, 2016). *See also Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, 457 F.3d 1284, 1292 (Fed. Cir. 2006) ("[R]eading an additional limitation from a dependent claim into an independent claim would not only make that additional limitation superfluous, it might render the dependent claim invalid…."). Thus, the presumption of claim differentiation is "especially strong when the limitation in dispute is the only meaningful difference between an independent and dependent claim…." *See Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 806 (Fed. Cir. 2007).

Here, the specification teaches that NR can come from three potential sources:

[22] Construction is necessary because it is undisputed that Elysium's NR ingredient is chemically synthesized. Claim 2 is the only asserted claim of the '086 patent; the PTAB found that all other claims of the '086 were invalid as anticipated by prior art published a century ago.

> The source of the nicotinamide riboside can be ***from a natural or synthetic source*** identified by the method of the instant invention, ***or can be chemically synthesized using established methods***. (Tanimori (2002) *Bioorg. Med. Chem. Lett.* 12:1135-1136; Franchetti (2004) *Bioorg. Med. Chem. Lett.* 14: 4655-4658."

'807 patent at 28:38-63 (emphasis added). Said another way, NR can come (1) from a natural source; (2) from a synthetic source; or (3) be chemically synthesized. "Isolated from a natural or synthetic source" is narrower than the NR of claim 1, because it excludes NR that has been chemically synthesized. The specification thus draws a clear distinction between NR isolated from "a synthetic source" and NR that is "chemically synthesized."

The specification further teaches that chemical synthesis includes extraction or purification steps, indicating that the use of such methods to produce NR is to be understood as different from isolating NR from a synthetic source. The patent directs the POSA to two references, Tanimori and Franchetti, that are said to describe "established methods" of chemically synthesizing NR. *Id.* As Dr. Adams explains, both Tanimori and Franchetti's chemical synthesis methods explicitly include steps to purify or extract the NR. Ex. 12 at ¶¶ 29-30. In Tanimori, the NR is purified by chromatography on activated charcoal and crystallization. *Id.*; Ex. 14 (Tanimori) at 1135. In Franchetti, the synthesis product is "purified by chromatography on activated charcoal and isolated as a white solid." Ex. 12 at ¶ 30; Ex. 15 (Franchetti) at 4656.

Plaintiffs' claim construction argument would have the Court treat purification or extraction of NR during the synthesis process as something other than chemical synthesis, contrary to the teaching of Tanimori and Franchetti. According to Plaintiffs, chemical synthesis creates only the intermediate product, whereas the purification step constitutes "isolating the NR from a synthetic source." *Supra,* at 44. The result, according to Plaintiffs, is that the NR is "*both* chemically synthesized *and* isolated from a synthetic source," such that chemically synthesized NR falls within both claim 1 and claim 2. *Id.* at 51-52. This tortured argument has one purpose: to rewrite claim 2 to cover Elysium's accused product, which Plaintiffs know is chemically synthesized.

To support their argument, Plaintiffs ignore the specification, disregard Tanimori and Franchetti's teachings, and rely entirely on extrinsic evidence from 2019, which obviously can have no bearing on interpretation of patents claiming 2004 and 2005 priority dates. *See Markman v. Westview Instrs., Inc.*, 52 F.3d 967, 986 (Fed. Cir. 1995) (en banc) ("the focus is on… what one of ordinary skill in the art at the time of the invention would have understood the term to mean"). A POSA reading the specification would understand that, in describing chemical synthesis by "established methods," the patent was referring to the entire process described in the two cited references. Plaintiffs offer no contrary expert opinion. Indeed, they offer no evidence that, as of the patents' priority date, there were any known methods to

make NR that did not include a purification step, a step they now claim amounts to "isolation from a synthetic source."

The specification thus confirms that "isolated from a natural or synthetic source" ***excludes*** NR obtained through chemical synthesis, a process described as including purification or extraction steps.[23] Elysium's construction is faithful to the intrinsic evidence; Plaintiffs' construction ignores it.

SkinMedica, Inc. v. Histogen, Inc., 727 F.3d 1187 (Fed. Cir. 2013) is instructive. In that case, the parties disputed the meaning of the claim term "culturing cells in three-dimensions" and whether it included the use of beads. The Federal Circuit began by noting that that the ordinary meaning of the term "would reach the use of beads." *Id.* at 1195. It nevertheless affirmed the district court's exclusion of beads from the scope of the claim because in their specification, "the patentees plainly and repeatedly distinguished culturing with beads from culturing in three-dimensions." *Id.* at 1196. The specification evidenced "a clear intent to distinguish between three dimensional culturing and culturing… on beads." *Id.* at

[23] To obtain NR that is not chemically synthesized, the patentee identified multiple natural and synthetic sources from which NR can be isolated. The specification states that "[n]atural sources… include, but are not limited to, cow's milk, serum, meats, eggs, fruit and cereals." *Id.* at 27:42-45. It states that "synthetic sources of nicotinamide riboside can include any library of chemicals commercially available from most large chemical companies…." '807 patent at 27:39-41. Nowhere does the specification state that a "synthetic source" of NR would be chemically-synthesized NR.

1197. So too here, the patents' specification expressly distinguishes isolation "from a natural or synthetic source" from obtaining the NR through "chemical synthesis."

Plaintiffs' construction would vitiate the distinction between claim 1 and claim 2. Under Plaintiffs' theory, chemically synthesized NR would always satisfy the source limitation in claim 2, because whenever NR is chemically synthesized, the product of the synthesis will have been isolated from a synthetic source. Because dependent claim 2 would not "narrow the scope of the claim from which it depend[s]," Plaintiffs' construction would render it invalid. *Amgen*, 2016 U.S. Dist. LEXIS 164744 at *9.

b. Dartmouth Agrees that Claim 2's Source Limitation Excludes Chemically Synthesized NR

Dartmouth endorsed Elysium's proposed construction of claim 2 in the IPR proceedings. Dartmouth admitted, "[c]laim 2 is narrower than Claim 1 because it further specifies that the nicotinamide riboside 'is isolated from a natural or synthetic source,' ***to the exclusion of chemically synthesizing the compound***. *See* '807 patent at 28:58-63." Ex. 5 at 13 (emphasis added). Dartmouth further explained, in distinguishing claim 2 from claim 1, that isolation from a natural or synthetic source refers to a methodology for obtaining NR from a chemical library or from a natural product:

> [The specification] provide[s] background and context for how a person of ordinary skill in the art ***would obtain nicotinamide riboside that is not chemically synthesized***…. [T]he specification identifies various

> synthetic and natural sources from which nicotinamide riboside can be isolated: 'Synthetic sources or nicotinamide riboside can include any library of chemicals commercially available from most large chemical companies…. Natural sources which can be tested for the presence [] of nicotinamide riboside include, but are not limited to, cow's milk, serum, meats, eggs, fruit and cereals. '807 patent, at 27:39-45.

Id. at 10 (emphasis added).

c. Dartmouth Disclaimed Chemically Synthesized NR

Faced with these admissions, Plaintiffs argue they should be disregarded unless they rise to the level of a prosecution history disclaimer. As a preliminary matter, even "prosecution history statements [that] do not rise to the level of unmistakable disavowal… do inform the claim construction." *Shire Dev., LLC v. Watson Pharms., Inc.*, 787 F.3d 1359, 1366 (Fed. Cir. 2015) (reversing district court construction of claim despite agreeing that no prosecution disclaimer occurred). At minimum, Dartmouth's statements constitute party admissions and inform the Court's claim construction analysis.

In any event, there was a prosecution history disclaimer. Prosecution disclaimer is particularly significant when it occurs in IPR proceedings, serving to protect the integrity of the judicial process by "ensur[ing] that claims are not argued one way in order to maintain their patentability and in a different way against accused infringers." *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1360 (Fed. Cir. 2017).

Dartmouth's statements during the IPR proceedings were "both clear and unmistakable." *See id.*at 1362. Dartmouth could not have been clearer in asserting to the PTAB that claim 2 "specifies that the nicotinamide riboside 'is isolated from a natural or synthetic source,' to the exclusion of chemically synthesizing the compound." Ex. 5 at 13. Dartmouth explained, over nearly two pages, how isolating NR from a natural or synthetic source means identifying NR in natural sources, such as milk or eggs, or in synthetic sources, such as commercially available chemical libraries. *Id.* at 9-10. The specification, Dartmouth argued, teaches that claim 2 is limited to "obtain[ing] isolated nicotinamide that is ***not*** chemically synthesized." *Id.* at 10 (emphasis added).

Plaintiffs contend that Dartmouth's statements were not clear and unmistakable, claiming that Dartmouth merely excluded from claim 2 NR that is chemically synthesized "without any separation or extraction step (for example, where the NR is used along with the other reaction products)." *Supra*, at 48. This is nonsense. Dartmouth said no such thing to the Patent Office. Moreover, claim 1 of the '807 patent, from which claim 2 depends, ***already*** requires that the NR be "isolated." Thus, the NR of both claim 1 and claim 2 is subjected to a separation step.

In addition, as discussed above, the specification cites to Tanimori (2002) and Franchetti (2004) as examples of chemical synthesis methods that are not "from a

natural or synthetic source." In the '807 IPR, Dartmouth cited that portion of the specification in explaining that chemically synthesized NR is outside the scope of claim 2. Ex. 5 at 9. Since both Tanimori and Franchetti include purification steps, Dartmouth could not have been referring to chemical synthesis "without any separation or extraction step." Plaintiffs' assertion to this Court that Dartmouth meant otherwise does not pass the blush test.

Finally, Plaintiffs argue that Dartmouth's statements are not "clear and unmistakable" because the Patent Office supposedly "rejected" them. *Supra*, at 48-49. That is false. Plaintiffs cite nothing in the PTAB's institution decision on the '807 patent that rejected Dartmouth's differentiation of claims 1 and 2. Rather, the PTAB's decision was based on construing "is isolated"—a limitation present in both claims 1 and 2—as imposing a 25% purity requirement. It did not discuss at all the "from a natural or synthetic source" limitation of claim 2. Similarly, in the '086 patent IPR decision, the PTAB again focused on "is isolated" to support its 25% purity requirement and did not construe "from a natural or synthetic source." Ex. 3 at 12-15.

d. Plaintiffs' Claim Differentiation Theory Finds No Support in the Specification or Caselaw

Bowing to Section 112 and the doctrine of claim differentiation, Plaintiffs acknowledge that claim 2 of both patents must be different from and narrower than claim 1 of those patents. Their theory explaining how their construction

accomplishes this is convoluted at best. They argue that claim 2 narrows claim 1 by excluding NR compositions that are merely "substantially free" from other components. Their proposed construction of claim 2 would make the following change from their construction of claim 1:

> "nicotinamide riboside that is separated ~~**or substantially free**~~ from at least some of the other components associated with the source of the molecule such that the weight of the nicotinamide riboside is at least 25% of the total weight of the nicotinamide riboside and any other components associated with the source of the molecule in said composition."

See supra, at 22, 41. Plaintiffs offer no support for construing "from a natural or synthetic source" in claim 2 as having the intended effect of removing the "or substantially free" language in claim 1. Plaintiffs' theory is wholly unmoored from the specification or the words "from a natural or synthetic source."

To make this argument, Plaintiffs are forced to construe "is isolated" a second time, giving it one meaning in claim 1 and a different meaning in claim 2. *See supra*, at 42-43. Their proposed construction would lead to the result that the same word, "isolated," would mean different things in an independent claim and in a second claim that depends from the first. It also ignores the words "from a natural or synthetic source" and gives this source limitation no effect. Plaintiffs cite no caselaw or evidence to support such an improbable interpretation.

Nor is there any merit to Plaintiffs' argument that the Court should construe claim 2 by considering the parties' current manufacturing processes, which long

post-date the patents. Their assertion that *Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322 (Fed. Cir. 2006) approves such an approach could not be more wrong. It is *en banc* Federal Circuit law that claims must be "construed without reference to the accused device." *SRI Int'l v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1118 (Fed. Cir. 1985) (en banc). *Wilson* did not overrule this *en banc* precedent. All *Wilson* stands for is that a court must understand why the issues in the case necessitate claim construction to ensure that it does not "assume[]… attributes of a proceeding seeking an advisory opinion." *Wilson*, 442 F.3d at 1327. As numerous courts have held, *Wilson* does not authorize construing claims to fit the accused device as Plaintiffs urge. *E.g. Fitness Anywhere LLC v. Woss Enters.*, 2015 U.S. Dist. LEXIS 156807, at *13-14 n.3 (N.D. Cal. Nov. 19, 2015); *U.S. Ethernet Innovations LLC v. Acer Inc.*, 2011 U.S. Dist. LEXIS 73935, *17 (N.D. Cal. Jul. 8, 2011). The Federal Judicial Center's "Patent Case Management Judicial Guide" explains, "knowing the context of the infringement (or validity) dispute gives courts a better sense of whether they even need to construe a term…. Nonetheless, the accused device has no relevance to how a person having ordinary skill in the art would interpret claim terms." FJC, PATENT CASE MANAGEMENT JUDICIAL GUIDE, 5.1.3.4 (3rd ed., 2016).

3. ChromaDex's Reply Position

Elysium's fundamental error is its assumption that "[t]he specification describes three *distinct* sources of NR: (1) natural sources, such as cow's milk; (2) synthetic sources, such as commercially available chemical libraries; and (3) chemically-synthesized NR." The specification, however, does not state or otherwise suggest that these categories cannot overlap (e.g., if the NR molecule were both from a "synthetic source" and "chemically synthesized"). As demonstrated below, that position would make no sense.

One of the disclosed sources of NR is a natural source such as milk. '807 patent, 27:42-45. In other words, milk is a broth that contains NR along with other components, such as proteins and fats. If NR is isolated from these other components of the broth, then that NR is "isolated from a natural source."

Another disclosed source of NR is a synthetic source. One synthetic source of NR is a broth containing NR that is created by chemical synthetic reactions (i.e., created by a chemical synthesis). This broth that contains NR (along with other products of the *synthetic* reactions) is, by definition, a "*synthetic* source" of NR. And if NR is isolated from the other components of that broth, then that NR is "isolated from a synthetic source." But it is also "chemically synthesized," since it was created, along with the other components of the broth, by chemical synthesis.

Tanimori and Franchetti disclose processes along these lines, in which a broth containing NR is synthesized, and then the NR is isolated from that broth. Notably, these papers expressly recognize the distinction between the chemical synthesis of the NR and the isolation of that NR from the broth created by the chemical synthesis. Franchetti, for example, reports that the authors "repeated th[e] synthetic strategy" disclosed by Tanimori, "but all attempts to isolate the [NR] were unsuccessful," thus making clear the distinction between synthesizing the NR (as part of the product mixture) and isolating the NR from that product mixture. Ex. 15 at 4656. Similarly, both ChromaDex and Elysium use manufacturing processes in which synthetic reactions create a product mixture containing NR, with subsequent steps to isolate the NR from that product mixture, yielding "chemically synthesized" NR that is "isolated from a synthetic source." *See* Ex. 7 at CDXDE_000002257–CDXDE_000002258; Ex. 8 at ELY_0077603-ELY_0077604; Ex. 9 at AMPAC0000681-AMPAC0000688; *Wilson Sporting Goods*, 442 F.3d at 1326-27 ("knowledge of [an accused] product or process provides *meaningful context* for the first step of the infringement analysis, claim construction").

Elysium incorrectly argues that the reason the NR of dependent claim 2 is narrower than the NR of independent claim 1 is that the NR of claim 2 "excludes NR that has been chemically synthesized." *Id.* That cannot be right, since the recited NR that is "isolated from a … synthetic source" may itself be chemically

synthesized, as demonstrated above. Instead, claim 2 is narrower than claim 1 because it excludes NR that is not "isolated from a natural or synthetic source."[24] For example, a chemically synthesized product mixture containing NR that has not been subject to a subsequent isolation step would contain NR that is not isolated from a synthetic source, and a composition containing the mixture would not satisfy claim 2's limitation that the NR is "isolated from a natural or synthetic source." Such a composition could still fall within claim 1 if the NR in the product mixture met the requirements for "isolated nicotinamide riboside," such as the 25% purity requirement. Although Elysium asserts that "whenever NR is chemically synthesized, the product of the synthesis will have been isolated from a synthetic source," this is clearly not true: just as NR in a natural product (milk) need not be isolated, so too NR in a synthesized product (the product mixture of a chemical synthesis) need not be subjected to a subsequent isolation step. That Elysium (like ChromaDex) chooses to use NR that is isolated from a synthetic source instead reflects a deliberate choice, based on the patented invention here, arising from the

[24] Thus, under ChromaDex's proposed claim constructions, the isolated NR of claim 1 may be either "separated or substantially free" from the other components associated with its source, whereas the NR of claim 2 must be "separated from" (*i.e.*, "isolated from") the other components associated with its source. Elysium argues that these constructions improperly give "the same word, 'isolated,'" different meanings between claims 1 and 2, but Elysium overlooks that claim 1 recites "isolated nicotinamide riboside," whereas claim 2 recites the different term, "the nicotinamide riboside is isolated from a natural or synthetic source."

inventor's recognition of the surprising and unexpected benefits of administering a composition with isolated NR.

Elysium similarly misunderstands the specification's reference to Tanimori and Franchetti. Elysium asserts that, "in describing chemical synthesis by 'established methods,'" such as Tanimori and Franchetti, "the patent was referring to the entire process described in [those] references." According to Elysium, because "both Tanimori and Franchetti's chemical synthesis methods explicitly include [purification] steps," the specification "teaches that chemical synthesis includes extraction or purification steps."

There is no basis, however, for Elysium's assertion that the specification refers to "the entire process described in" Tanimori and Franchetti as chemical synthesis. To the contrary, Franchetti expressly recognized that the synthesis of NR is distinct from the isolation of NR from the chemically synthesized broth. Ex. 15 at 4656 (stating that the authors "repeated th[e] synthetic strategy" disclosed by Tanimori "but all attempts to isolate the [NR] were unsuccessful"). Nothing in the patent's reference to Tanimori and Franchetti for the chemical synthesis contradicts this well-understood distinction between synthesizing NR and isolating it.

Elysium's citation of *SkinMedica* is inapposite. In *SkinMedica,* the claim term at issue was "culturing ... cells in three-dimensions," but "the patent expressly confine[d] culturing with beads to two-dimensional culturing"—a category that was

mutually exclusive with three-dimensional culturing. 727 F.3d at 1194, 1199. Here, by contrast, the specification does not define or characterize NR isolated from a synthetic source and chemically synthesized NR as mutually exclusive categories, since NR can be *both* "isolated from a synthetic source" and "chemically synthesized."

Finally, Elysium erroneously interprets Dartmouth's statements in the IPRs. Dartmouth stated in the IPR that "[c]laim 2 is narrower than claim 1 because it further specifies that the nicotinamide riboside 'is isolated from a natural or synthetic source,' to the exclusion of chemically synthesizing the compound." Ex. 5 at 13 (citing '807 patent, 28:58-63). Contrary to Elysium's mischaracterizations, Dartmouth did not disclaim NR that is isolated from a chemically synthesized broth, since such NR would be both "isolated from a synthetic source" and "chemically synthesized." Instead, Dartmouth's statement is more naturally read to mean that claim 2 excludes NR that is chemically synthesized but not "isolated from a natural or synthetic source." Elysium, therefore, has not come close to showing a "clear and unmistakable" disclaimer of NR that is isolated from a chemically synthesized broth. *See Aylus Networks*, 856 F.3d at 1359.[25]

[25] Additionally, the PTAB rejected Dartmouth's allegedly disclaiming statements, and Dartmouth acquiesced in the PTAB's rejection. *See Ecolab*, 569 F.3d at 1343. Elysium disagrees, but it overlooks that the PTAB rejected Dartmouth's proposed

4. Elysium's Sur-Reply Position

Plaintiffs concede the patents disclose three sources of NR. They are listed in the disjunctive: NR can have a natural source, a synthetic source, "***or*** can be chemically synthesized." '807 patent, 28:58-61. Despite this, Plaintiffs argue that the three sources are non-distinct and can overlap.

This argument contradicts Dartmouth's own representations to the Patent Office. Dartmouth admitted that "[c]laim 2 is narrower than claim 1 because it further specifies that the nicotinamide riboside 'is isolated from a natural or synthetic source,' ***to the exclusion of chemically synthesizing the compound***." Ex. 5 at 13 (emphasis added). No statement could contradict Plaintiffs' litigation position more emphatically than this.

Plaintiffs' argument also fails to differentiate claim 2 of the '807 patent from claim 1. With no citations to intrinsic evidence or expert declaration, Plaintiffs simply assert that a POSA would understand claim 2 to exclude only a chemical "broth" of NR that has undergone no purification or separation steps. *See supra*, at 63-64. This is nonsense. Claim 1 of the '807 patent ***already requires*** that the composition comprise "isolated" NR. Thus, not even claim 1 would cover Plaintiffs'

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construction of "is isolated from a natural or synthetic source" to mean "fractionated from other cellular components," and that the PTAB therefore rejected Dartmouth's arguments in support of that proposed construction, including the alleged disclaiming statements.

hypothetical "broth." *See Intamin, Ltd. v. Magnetar Techs., Corp.*, 483 F.3d 1328, 1335 (Fed. Cir. 2007) ("An independent claim impliedly embraces more subject matter than its narrower dependent claim.").

As Dr. Adams testified—without contradiction—a POSA understands that chemical synthesis of a compound invariably will include purification steps. Ex. 28 at 150-51 ("[I]n order to do chemistry, you have to isolate and purify…. That's what chemistry is all about. You know, you don't just give somebody a… pot full of a mixture of things and say, here's the drug that you take.").

This is evident from the specification. It cites two papers, Tanimori and Franchetti, as exemplifying NR that is "chemically synthesized using established methods." '807 patent, 28:58-63. Both include purification steps. The patent does not cite these papers as examples of NR "isolated from a synthetic source." On the contrary, as noted above, it uses them to distinguish chemically synthesized NR from NR identified from a natural or synthetic source.

In fact, the inventor went to great lengths to describe what he meant by isolating NR "from a synthetic source." In column 4, he explained that the "present invention is further a method for identifying a natural or synthetic source for nicotinamide riboside." '807 patent, 4:8-9; 27:12-14. He explained that this involved creating a cell "lacking a functional glutamine-dependent NAD+ synthetase" and contacting it with an extract from a natural or synthetic source. *Id.*

at 4:10-15; 27:14-17. If the cell grew, that indicated the presence of NR. *Id.* at 4:15-19; 27:35-38. The patent then describes synthetic sources from which NR can be isolated using this method as including "any library of chemicals commercially available from most large chemical companies." *Id.* at 27:39-41. By contrasting the isolation of NR from a synthetic source with chemical synthesis of NR, the inventor drew a sharp distinction between the two. Independent claim 1 encompasses all three sources of NR, but dependent claim 2 excludes chemical synthesis of NR, just as Dartmouth explained to the PTAB in 2017, before Plaintiffs commenced this litigation and needed a new construction of claim 2 to support infringement.

D. "in combination with one or more of tryptophan, nicotinic acid, or nicotinamide"

TERM (PATENT/CLAIMS)	CHROMADEX'S PROPOSED CONSTRUCTION	ELYSIUM'S PROPOSED CONSTRUCTION
"in combination with one or more of tryptophan, nicotinic acid, or nicotinamide" '807 Patent: Claim 1	"both isolated nicotinamide riboside and one or more of tryptophan, nicotinic acid, or nicotinamide are found in the composition"	"…and is formulated using a process of combining 1) the isolated nicotinamide riboside with 2) tryptophan, nicotinic acid, or nicotinamide"

1. ChromaDex's Opening Position

ChromaDex's proposed construction accords with the claim term's plain and ordinary meaning. Claim 1 recites that the claimed composition comprises one component (isolated NR) "in combination with" a second component (tryptophan,

nicotinic acid, and/or nicotinamide). The claim thus requires only that both components be found in the composition. Indeed, when the patentee added this claim term to the claims pending in prosecution, it explained that, "[i]n accordance with certain embodiments of the present invention, the composition further *includes* tryptophan, nicotinic acid, and/or nicotinamide. … Applicant has amended claim 30 to read on the *inclusion* of one or more of tryptophan, nicotinic acid, or nicotinamide in the instant composition." Ex. 10 at 4-5 (citations omitted).

Elysium's proposed construction impermissibly seeks to import a process limitation into claim 1, in an attempt to avoid infringement. Specifically, Elysium attempts to limit the recited "composition" to only those compositions that are "formulated using a *process* of combining 1) the isolated nicotinamide riboside with 2) tryptophan, nicotinic acid, or nicotinamide," without any support whatsoever in the intrinsic evidence.[26] This is improper. *See AFG Indus., Inc. v. Cardinal IG Co.*, 375 F.3d 1367, 1372 (Fed. Cir. 2004) ("Cardinal asks this court to adopt a new construction of the claim that would impermissibly import a process limitation into a pure product claim."); *see also Thorner*, 669 F.3d at 1367.

[26] Elysium's argument here is also inconsistent with its argument in the IPRs that the NR in milk was "in combination with" tryptophan and nicotinamide merely because the tryptophan and nicotinamide also happened to be present. Ex. 11 at 13.

Elysium's proposed construction is also improper because the specification discloses that tryptophan, nicotinic acid, or nicotinamide can be present in the inventive compositions without being affirmatively combined with the isolated NR. The specification discloses, for example, that the "[s]afety, specificity and efficacy of [particular disclosed] treatments can be modulated by supplementation with *or restriction of* the amounts of any of the NAD+ precursors, namely tryptophan, nicotinic acid, nicotinamide, or nicotinamide riboside." '807 patent, 25:14-23. Consequently, not only may tryptophan, nicotinic acid, or nicotinamide be added to the inventive compositions, but those ingredients may also be "restrict[ed]." Contrary to Elysium's position that tryptophan, nicotinic acid, or nicotinamide must be affirmatively combined with the isolated NR, this disclosure shows that the invention includes compositions in which tryptophan, nicotinic acid, or nicotinamide were already present in the composition, as a result of the chemical synthesis that created the NR or otherwise.[27]

2. Elysium's Answering Position

The claims of the '807 patent require a composition comprising isolated nicotinamide riboside "in combination with one or more of tryptophan, nicotinic acid, or nicotinamide." Construing this to mean, as Elysium proposes, that the

[27] For example, [redacted].

composition is formulated using a process of combining the isolated nicotinamide riboside with any of tryptophan, nicotinic acid, or nicotinamide comports with the specification, the prosecution history, and the understanding of a POSA.

The meaning of this claim language is at issue because Plaintiffs contend that small amounts of nicotinamide inherently present in any NR composition, either as degradation products or impurities, satisfy this claim limitation, even in the absence of any actual combining of isolated NR with nicotinamide.[28] As discussed below, Plaintiffs' construction would effectively write this limitation out of the claim.

a. A POSA Would Understand that Any NR Composition Will Contain Some Nicotinamide as a Degradation Product or Impurity of Chemical Synthesis

As Dr. Adams explains, nicotinamide is a degradation product of NR. Ex. 12 at ¶¶ 21-26. Any NR composition will contain nicotinamide due to the breakdown of a bond in NR's chemical structure by atmospheric humidity, through a process called hydrolysis. *Id.* This has been understood for decades, and is described in a 1978 paper by Ferraz and colleagues. *Id.* In addition, the chemical reaction by which NR is synthesized uses nicotinamide as a starting material, which cannot be

[28] None of tryptophan, nicotinic acid, or nicotinamide is listed as an ingredient on the label of either Elysium's accused product or ChromaDex's allegedly embodying product. Ex. 20 (Elysium label); Ex. 17 (ChromaDex label).

fully removed from the synthesis product. *Id.* at ¶¶ 27-30. The Tanimori and Franchetti papers cited in the specification as examples of "established methods" for chemically synthesizing NR (*see* '807 patent at 28:58-63), both use nicotinamide as a starting material. *See* Ex. 12 at 29-30. As Dr. Adams describes, a POSA would understand that the NR composition created by using Tanimori's synthesis method, for example, would necessarily contain some nicotinamide as a degradation product or synthesis impurity. *Id.*

b. Elysium's Construction is Faithful to the Claims

Elysium's construction is faithful to the claims as a whole and gives the "in combination with" limitation meaning and purpose in the claim. ChromaDex's construction, by contrast, renders this claim element meaningless and creates dissonance both within claim 1 and with other claims of the closely-related '086 patent.

As explained above, a POSA would recognize that the "isolated nicotinamide riboside" element of claim 1 would necessarily include some nicotinamide as a degradation product or synthesis impurity. A POSA would also recognize that NR prepared using Tanimori and Franchetti's methods, as described in the specification, would contain some nicotinamide. Thus, a POSA would not interpret "in combination with…nicotinamide" to require only that nicotinamide be "found in" the composition, because a POSA would know that nicotinamide already would be

found in "isolated nicotinamide riboside." *See* Ex. 12 at ¶ 31. Under Plaintiffs' construction, ***any*** NR composition would satisfy the "in combination with…nicotinamide" limitation. It is axiomatic that "claims are interpreted with an eye toward giving effect to all terms in the claim." *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950-51 (Fed. Cir. 2006). The Federal Circuit has consistently rejected constructions that render a claim limitation "meaningless." *E.g. Id.* (collecting cases); *Cat Tech LLC v. TubeMaster, Inc.*, 528 F.3d 871, 885 (Fed. Cir. 2008).

Plaintiffs' construction also would require the Court to give two different terms within claim 1 of the '807 patent the same meaning: "in combination with" and "comprising."[29] Where patent claims use different words, they must be presumed to have different meanings, especially when those words are in the same clause. *See Ethicon Endo-Surgery, Inc. v. United States Surgical Corp.*, 93 F.3d 1572, 1579-80 (Fed. Cir. 1996) (refusing to treat two different phrases in the same claim as synonyms). Under Plaintiffs' proposed construction of claim 1, the term "in combination with" could be replaced by "comprising" and the meaning would be unchanged.

[29] Claim 1 begins with the words "[a] composition comprising." "Comprising" is an open-ended term of art meaning that the composition must include the named elements, but other unclaimed elements are also permitted. *E.g. Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir. 1997).

The "in combination with" language should also be read in light of the closely-related '086 patent, filed during prosecution of the '807 patent. In claim 4 of the '086 patent, Dartmouth claimed an NR composition "further ***comprising*** one or more of tryptophan, nicotinic acid, or nicotinamide." (emphasis added). Claim 4 was found invalid in the IPR because the PTAB agreed that the presence of nicotinamide was inherent in prior art compositions of NR. Ex. 3 at 28-29. Dartmouth's choice of "comprising" language in claim 4 of the '086 patent with reference to the same three NAD+ precursors identified in claim 1 of the '807 patent underscores that Dartmouth's use of "in combination with" in the '807 patent was deliberate and has a different meaning than "comprising." *See Forest Labs., Inc. v. Teva Pharms. USA, Inc.*, 2016 U.S. Dist. LEXIS 322, at *22-23 (D. Del. Jan. 5, 2016).

c. Elysium's Construction is Faithful to the Specification

Elysium's construction is also faithful to the specification, which confirms that tryptophan, nicotinic acid, or nicotinamide must be separately combined with the isolated nicotinamide riboside. In column 29, the specification describes administering an "effective amount of nicotinamide riboside" to a patient and "adjust[ing] accordingly" the "dosages" of NR in response to the patient's symptoms. As discussed above, a POSA would understand that such an NR

composition (like any NR composition) would inherently contain some nicotinamide.

Immediately after that paragraph, from lines 19-23, the specification describes a further "alteration" beyond merely changing the dosage of the NR. It states:

> As alterations of NAD+ metabolism may need to be optimized for particular conditions, it is contemplated that nicotinamide riboside treatments can further be used ***in combination with*** other NAD+ precursors, e.g., tryptophan, nicotinic acid and/or nicotinamide."

(emphasis added). This passage proposes further alterations to "optimize" the NR treatments described in the prior paragraph. It describes that the further, optimizing alterations are using the NR treatment "in combination with" tryptophan, nicotinic acid, or nicotinamide. In this context, it is clear that the patentee was proposing to formulate an alternative composition for NR treatments by combining the NR with added nicotinamide or another NAD+ precursor. This passage would make no sense if its reference to combining NR with nicotinamide meant nicotinamide that was present in the isolated nicotinamide riboside all along. *See* Adams Dec. ¶¶ 32-33.[30]

[30] Plaintiffs do not even cite this passage in their opening brief. The only part of the specification they do cite (25:14-23) as support for their position is irrelevant. That passage concerns "nicotinamide riboside-related prodrugs" used to treat cancer that can be modulated with NAD+ precursors. The '807 patent does not claim NR-related prodrugs. In addition, the passage cited by Plaintiffs makes no mention of the phrase "in combination with" and cannot shed light on it.

This Court need not take Elysium's word for it. In the '086 IPR, Dartmouth's counsel, discussing the same portion of the specification in the '086 patent, agreed that it described ***adding*** nicotinamide to an NR composition:

> [T]he second paragraph there says that you can ***add*** some of these other compounds [i.e. tryptophan, nicotinic acid, or nicotinamide] if you want to alter NAD+ metabolism. So you can ***add those compounds*** to another compound or ***to another composition where nicotinamide riboside is the active agent***.

Ex. 21 (IPR Oral Arguments) at 42 (emphases added). The Court should reject Plaintiffs' attempt to sow confusion about the meaning of "in combination with" and recognize Plaintiffs' argument as an overreaching attempt to cover an accused product in which no such combination occurs.

d. Elysium's Construction is Confirmed by the Prosecution History

The prosecution history reinforces the conclusion that "in combination with one or more of tryptophan, nicotinic acid, or nicotinamide" requires a composition formulated using a process of combining two separate elements into one composition: (1) isolated NR and (2) an NAD+ precursor such as nicotinamide. It shows that the claim limitation was not meant to capture an NR composition merely because it contains trace amounts of nicotinamide intrinsically present in all NR, including NR made using Tanimori's "established method."

In fact, the prosecution history shows that Tanimori was central to the genesis of the "in combination with" limitation. The limitation was added specifically to

overcome a rejection over Tanimori. In an April 2010 office action, the examiner rejected Dartmouth's claims to NR compositions, which at the time required only "isolated nicotinamide riboside." Ex. 22. The examiner argued that Tanimori disclosed "chemical synthesis… of nicotinamide riboside and analogues" and taught that NR was an NAD+ precursor. *Id.* at 4. He reiterated this position in an August 2010 advisory action, arguing that the application "does not teach a mechanism of action of nicotinamide riboside outside of what is known in the art." Ex. 23 at 2 (Aug. 2010 Advisory Action).

In response, Dartmouth limited the claims to require that the isolated NR be "in combination with one or more of tryptophan, nicotinic acid, or nicotinamide." Ex. 10 at 3. Dartmouth disputed the examiner's assertion that the application did not teach a new mechanism of action for NR. Dartmouth argued, "[t]he instant specification teaches that NAD+ metabolism in mammals can be modulated with a composition containing nicotinamide riboside." Ex. 10 at 4. This was done by creating compositions "***further*** includ[ing] tryptophan, nicotinic acid, and/or nicotinamide." *Id.* at 4-5 (emphasis added). For support, Dartmouth cited to page 58, lines 14-18 of the original specification. *Id.; see also* Ex. 24 (Original Specification) at 58. This is the same passage discussed above describing "further" alterations to "optimiz[e]" NR treatments by "combining" them with tryptophan, nicotinic acid, and/or nicotinamide. Relying on its claim amendment, Dartmouth

argued that Tanimori did not teach a "composition, which ***is formulated as*** presently claimed." Ex. 10 at 5 (emphasis added). If this argument to overcome Tanimori is to make any sense, "in combination with" must mean formulating the composition by combining the NR with added nicotinamide or another NAD+ precursor. Under Plaintiffs' contrary construction, Dartmouth's amendment did absolutely nothing to distinguish its amended claims from Tanimori.

The examiner, in response, made clear he understood the amendment to mean adding an NAD+ precursor to the isolated NR. In initially rejecting the patentability of the amended claims, he wrote that "***supplementing*** the effect of nicotinamide riboside with tryptophane and/or niacin would have been obvious…." Ex. 25 at 4 (emphasis added).[31]

This prosecution history strongly supports Elysium's construction. Under Elysium's construction, Dartmouth's argument and the examiner's responses make sense: Dartmouth sought to overcome Tanimori by arguing that the amended claims covered a composition formulated to supplement the effect of NR by the addition of NAD+ precursors like nicotinamide. Under Plaintiffs' construction of "in combination with… nicotinamide," by contrast, Dartmouth's amendment to add this claim limitation would not alter the claim scope and would render Dartmouth's

[31] Niacin contains both nicotinamide and nicotinic acid. *See* '807 patent at 8:55-60.

arguments distinguishing Tanimori nonsensical to a POSA. Plaintiffs' attempt to take back through claim construction the claim scope that Dartmouth purposefully gave up when it obtained allowance of the claims over Tanimori should be rejected.

3. ChromaDex's Reply Position

Rather than apply the claim term's plain and ordinary meaning, Elysium impermissibly seeks to import a process limitation into this composition claim. *See AFG Indus.*, 375 F.3d at 1372; *Thorner*, 669 F.3d at 1367. Notably, Elysium's argument is inconsistent with its argument in the IPRs that NR was "in combination with" tryptophan and nicotinamide merely because tryptophan and nicotinamide are also present in milk. Ex. 11 at 13. Elysium attempts to prop up its improper construction by arguing that nicotinamide is necessarily present in NR compositions and that its proposed construction is supported by the intrinsic evidence, but these arguments are meritless.

a. Even If All NR Compositions Contain Trace Amounts of Nicotinamide, that Does Not Support Departing from the Claim Term's Plain and Ordinary Meaning

Elysium argues that interpreting "'in combination with … nicotinamide' to require only that nicotinamide be 'found in' the composition" would render the limitation meaningless because all NR compositions contain nicotinamide as a degradation product. As Dr. Adams conceded, however, he did not quantify the rate at which NR degrades to nicotinamide, either generally or specifically in Elysium's

BASIS product. Ex. 28, 113:7-114:10, 115:17-117:8. In fact, Dr. Adams conceded that "[i]t certainly would be advisable to have a compound that doesn't degrade when you sell it to … consumers." *Id.*, 113:7-114:10.

Assuming for the sake of argument that Elysium is correct that NR compositions inevitably contain trace amounts of nicotinamide as a result of degradation, that is a red herring because [redacted], Ex. 31 at ELY_0019952. [redacted]. As Dr. Adams conceded during his deposition, the NR could be considered "in combination with" nicotinamide under such circumstances. Ex. 28, 141:2-142:3.

It is well established that claim terms need be construed "only to the extent necessary to resolve the controversy" between the parties. *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999); *see also Wilson*, 442 F.3d at 1326-27. Here, [redacted],

Dr. Adams's assertions regarding the degradation of NR to nicotinamide are irrelevant.

Elysium argues that ChromaDex's proposed construction would give the terms "in combination with" and "comprising" the "same meaning." Not so: "'Comprising' … means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." *Genentech*, 112 F.3d at 501. The "in combination with" term has the different meaning that both of the recited components are found in the composition.

Finally, the specification does not support Elysium's attempt to read a process limitation into claim 1. The specification discloses: "As alterations of NAD+ metabolism may need to be optimized for particular conditions, it is contemplated that nicotinamide riboside treatments can further be used in combination with other NAD+ precursors, e.g., tryptophan, nicotinic acid and/or nicotinamide." '807 patent, 29:19-23. Elysium argues that "the patentee was proposing to formulate an alternative composition for NR treatments by combining the NR with added nicotinamide or another NAD+ precursor," and that "[t]his passage would make no sense if its reference to combining NR with nicotinamide meant nicotinamide that was present in the isolated nicotinamide riboside all along." But Elysium overlooks that this disclosure could reasonably be read not to involve "combining the NR with added nicotinamide or another NAD+ precursor": the formulator could simply

choose not to remove from the composition the nicotinamide that would otherwise have been completely or mostly removed. As Dr. Adams recognized, the formulator could thereby create a formulation comprising NR "in combination with" nicotinamide without affirmatively adding nicotinamide to the composition. Ex. 28, 141:2-142:3.

This reading of the disclosure is consistent with Dartmouth's statement in the IPR that the disclosure teaches that "you can add some of these other compounds [*i.e.*, tryptophan, nicotinic acid, or nicotinamide] if you want to alter NAD+ metabolism." Dartmouth did not argue that this disclosure *requires* the NAD+ precursors to be affirmatively added to a composition, but simply that "you *can* add" the disclosed NAD+ precursors to the composition.

b. The Prosecution History Does Not Support Departing from the Claim Term's Plain and Ordinary Meaning

Elysium cites the applicant's arguments distinguishing Tanimori, but these arguments do not support its proposed construction. In connection with its amendment of the claims to add the "in combination with" limitation, the applicant explained:

> The instant specification teaches that NAD+ metabolism in mammals can be modulated with a composition containing nicotinamide riboside. In accordance with certain embodiments of the present invention, the composition further includes tryptophan, nicotinic acid, and/or nicotinamide. Accordingly, in an earnest effort to further distinguish the present invention from the teachings of the cited references [including Tanimori], Applicant has amended claim 30 to read on the

> inclusion of one or more of tryptophan, nicotinic acid, or nicotinamide in the instant composition.

Ex. 10 at 4-5 (citation omitted). The applicant further explained that "none of the primary or secondary references teach nor suggest a composition, which is formulated as presently claimed." *Id.* at 5.

These statements do not support Elysium's proposed requirement that the recited NAD+ precursors be affirmatively added to the isolated NR. The applicant never mentioned such a requirement, but instead explained that "the composition further *includes* tryptophan, nicotinic acid, and/or nicotinamide," and that the "in combination with" limitation caused the claim "to read on the *inclusion* of one or more of tryptophan, nicotinic acid, or nicotinamide in the instant composition." *Id.* at 4-5 (citation omitted).

Elysium asserts that, because Tanimori allegedly disclosed a composition comprising nicotinamide, the applicant's statement that Tanimori does not "teach nor suggest a composition, which is formulated as presently claimed," *id.* at 5, must have meant that Tanimori did not disclose affirmatively adding the NAD+ precursors to the NR. Elysium's assertion, however, is refuted by the record. There is no indication in the applicant's remarks that Tanimori taught a composition comprising nicotinamide, or even comprising a carrier. To the contrary, the examiner subsequently acknowledged that what "Tanimori do[es] *not* teach is the presence of

tryptophane, nicotinic acid or nicotinamide or the carrier compounds recited in claim 30." Ex. 36 at 4.

Finally, Elysium argues that the examiner "made clear he understood the amendment to mean adding an NAD+ precursor to the isolated NR" because he wrote that "supplementing the effect of nicotinamide riboside with tryptophane and/or niacin would have been obvious." (quoting Ex. 25 at 4). However, this statement is silent regarding nicotinamide, and even regarding tryptophan and niacin, a formulator could "supplement[] the effect" of NR by choosing not to remove tryptophane or niacin. At most, the examiner's statement indicates that affirmatively adding those NAD+ precursors was one way—not necessarily the only way—to satisfy the "in combination with" limitation.

4. Elysium's Sur-Reply Position

Plaintiffs do not dispute that nicotinamide is a significant degradation product of NR as well as an impurity inherently present in all chemically synthesized NR. Indeed, ChromaDex admitted in an FDA filing that at ambient temperature, stability testing of NR in solution "resulted in considerable degradation of NR into nicotinamide within a day (82.4% NR)." Ex. 38 at 19.[32] Plaintiffs likewise do not

[32] ChromaDex's report to FDA of nearly 20% degradation in a single day belies Plaintiffs' unsupported assertion that [redacted] "far exceeds" any nicotinamide that can result from degradation. The Court should reject Plaintiffs' improper invitation to

dispute Dr. Adams' testimony that as of the priority date a POSA would have understood that nicotinamide was a degradation product of NR and an impurity in all chemically-synthesized NR. Ex. 12 at ¶¶ 20-30.

Plaintiffs' construction, by which nicotinamide merely need be present in a composition to infringe the '807 patent, cannot be correct. Such construction would render the limitation "in combination with… nicotinamide" meaningless. As Dr. Adams explained in his deposition, "in combination with… nicotinamide" must mean "something on top of" nicotinamide already present in all NR as an impurity. Ex. 28 at 139 ("So nicotinamide is an impurity in nicotinamide riboside, but the patent, I think, they're making pretty clear that they're adding nicotinamide to that, in addition.").

Plaintiffs' arguments ignore the plain meaning of "combination," which is "a result or product of combining." *See* Ex. 39 (Webster's Third New International Dictionary (2002)). The Federal Circuit's decision in *Miken Composites, L.L.C. v. Wilson Sporting Goods Co*., 515 F.3d 1331 (Fed. Cir. 2008) is analogous. The court there rejected the patentee's argument that an "insert" in a claim to a softball bat was "purely structural, and that it does not matter whether an insert is placed into a pre-existing frame or whether a frame is built around it." *Id.* at 1335. Instead, the court

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construe the claims with reference to the accused product by considering the amount of nicotinamide in Elysium's product.

held that use of the word "insert" meant that the component had to be inserted into a pre-existing bat frame. *Id*. Similarly, "in combination with… nicotinamide" cannot be construed to include nicotinamide that was ***never combined with*** NR but rather is already there due to impurities in the isolated NR or its degradation. *See also Indivior Inc. v. Dr. Reddy's Labs., S.A.*, 752 F. App'x 1024, 1033 (Fed. Cir. 2018) ("[T]he claim term 'continuously cast film' does require a process—the film is made through continuous casting.").

In fact, "in combination with… nicotinamide" was added for a specific purpose: to overcome Tanimori. *See supra*, at 78-81. As Dr. Adams explains, and Plaintiffs do not contest, a POSA would have understood that Tanimori described a composition that comprised both NR and nicotinamide. Ex. 12 at ¶ 29. The Court's claim construction should reflect this prosecution history. For example, in *Chimie v. PPG Indus.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005), the Federal Circuit construed "atomized precipitated silica particulates" to require particles that had been pulverized and subjected to a liquid pressure nozzle. This is because the patentee added that claim term to overcome prior art that did not use such a process. *Id.* at 1384-85. So too here, where "in combination with… nicotinamide" was added to overcome Tanimori, it cannot be construed so broadly as to encompass the nicotinamide inherently present in Tanimori's NR.

E. "increases NAD+ biosynthesis upon oral administration"

TERM (PATENT/CLAIMS)	CHROMADEX'S PROPOSED CONSTRUCTION	ELYSIUM'S PROPOSED CONSTRUCTION
"increases NAD+ biosynthesis upon oral administration" '807 Patent: Claim 1	This term should be construed according to its plain and ordinary meaning, but if construction is necessary, it should be construed as: "increases NAD+ biosynthesis upon oral administration relative to the level of NAD+ biosynthesis if the composition were not administered"	"increases NAD+ biosynthesis in an animal upon oral administration as compared to oral administration of a composition comprising isolated nicotinamide riboside not in combination with tryptophan, nicotinic acid, or nicotinamide."

1. ChromaDex's Opening Position

The term "increases NAD+ biosynthesis upon oral administration" as recited in claim 1 of the '807 patent has a plain and ordinary meaning to a POSA. If the Court finds that construction is necessary, the term should be construed to mean that the claimed composition "increases NAD+ biosynthesis upon oral administration relative to the level of NAD+ biosynthesis if the composition were not administered." This construction is consistent with, and required by, the plain language of claim 1, which recites simply that the claimed "*composition* … increases NAD+ biosynthesis upon oral administration." Determining whether this claim

limitation is satisfied is straightforward: does oral administration of the claimed composition increase NAD+ biosynthesis, or not?

Elysium's proposed construction—which requires comparing the result of administering the claimed composition to the result of administering a composition found nowhere in the claim—finds no support in the claim language or the specification. It should therefore be rejected. *See Phillips*, 415 F.3d at 1312-15; *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

2. Elysium's Answering Position

Two aspects of this limitation in the '807 patent require construction: (1) whether the claims are directed to increasing NAD+ biosynthesis "in an animal," as Elysium contends, and (2) determining the comparator to measure the "increase" in NAD+ biosynthesis.

Plaintiffs do not offer any objection to the reference to "animals" in Elysium's construction.[33] The specification specifically describes oral administration of the formulated compositions to "an animal subject such as a human, agriculturally-important animal, pet or zoological animal." '807 patent at 32:19-23. There should be no dispute here.

[33] This aspect of claim construction is important to determine whether the specification sufficiently enables and describes an "animal" genus.

The second issue concerns the comparator to measure the "increase in NAD+ biosynthesis" required by claim 1. The patentee's language begs the question: an increase relative to what? Is it relative to administering no composition at all? Or is the increase relative to administering NR that is not in combination with tryptophan, nicotinamide, and/or nicotinic acid? The claim does not say.[34]

Construction is necessary because Plaintiffs contend that the '807 claims cover compositions containing trace amounts of nicotinamide inherent in any NR composition, either as impurities in chemical synthesis or as degradation products, even if the presence of nicotinamide in the composition does nothing to increase NAD+ biosynthesis. Elysium, by contrast, contends that the claims cover combination therapies where the nicotinamide is added in order to ***optimize*** NR treatments by increasing the NAD+ biosynthesis effects of those treatments.

The specification and prosecution history support Elysium's construction. The specification describes previously known combinations of NAD+ precursors and their synergistic effects, stating that "niacin as a mixture of nicotinamide and nicotinic acid may attest to the utility of utilizing multiple pathways to generate NAD+." '807 patent at 8:55-60. It continues, stating that "***supplementation***" of

[34] For this reason, Elysium contends that the claim is indefinite, an issue for another day.

these treatments "with nicotinamide riboside as a third importable NAD+ precursor can be beneficial for certain conditions." *Id.*

As discussed above, the specification then describes in column 29 the administration of treatments containing "[a]n effective amount of nicotinamide riboside." *Id.* at 29:11-18. It continues, stating that "[a]s alterations of NAD+ metabolism may need to be optimized for particular conditions, it is contemplated that nicotinamide riboside treatments can further be used in combination with other NAD+ precursors, e.g., tryptophan, nicotinic acid and/or nicotinamide." *Id.* at 29:19-23. This discussion makes clear that the combination of NR with other NAD+ precursors is intended to "optimiz[e]"nicotinamide riboside treatments" and that the "alterations of NAD+ metabolism" the patent describes are relative to the effect of "nicotinamide riboside treatments" that are not supplemented by the addition of another NAD+ precursor.

As discussed above, during prosecution, Dartmouth relied on its claim amendment adding the "in combination with" limitation to overcome Tanimori. In that connection, Dartmouth argued that the "specification teaches that NAD+ metabolism in mammals ***can be modulated***" by using the claimed combination of isolated NR with tryptophan, nicotinic acid, or nicotinamide. Ex. 10 at 4-5. The only way Dartmouth's amendment and argument make sense is if the increase in

NAD+ biosynthesis effected by the claimed combination is relative to treatment with NR alone.

3. ChromaDex's Reply Position

In contrast to the claim term's plain and ordinary meaning—that the claimed *composition* increases NAD+ biosynthesis upon oral administration[35]—Elysium's proposed construction contorts the term so that it incorporates a comparison with no basis in the intrinsic evidence.

Elysium cites the statement in the specification that, "[a]s alterations of NAD+ metabolism may need to be optimized for particular conditions, it is contemplated that nicotinamide riboside treatments can further be used in combination with other NAD+ precursors, e.g., tryptophan, nicotinic acid and/or nicotinamide." '807 patent, 29:19-23. But this does not support the strained comparison that Elysium attempts to graft onto the claim, under which the recited increase in NAD+ biosynthesis would be caused only by the recited NAD+ precursors, i.e., tryptophan, nicotinic acid and/or nicotinamide. Claim 1 recites that the claimed "composition"—not any one of its particular components—"increases NAD+ biosynthesis upon oral

[35] Similarly, the PTAB found that claim 5 of the '086 patent, which recites "[t]he pharmaceutical composition of claim 1 which increases NAD+ biosynthesis upon oral administration," requires "the *composition* of claim 1 to increase the biosynthesis of NAD+ production," not for any particular component of the composition "to necessarily cause the increased biosynthesis." Ex. 3 at 30.

administration." *Id.*, cl. 1. Indeed, the specification explains that the isolated NR, not just the recited NAD+ precursors, contributes to the recited increase in NAD+ biosynthesis. *See, e.g.*, *id.*, 28:45-47.

4. Elysium's Sur-Reply Position

In their arguments, Plaintiffs never explain why the increase in NAD+ biosynthesis for the combination product claimed in the '807 patent should be measured relative to administration of no composition at all. Tellingly, Plaintiffs point to nowhere in the specification in which a composition comprising NR in combination with tryptophan, nicotinic acid, or nicotinamide is assessed with respect to its effect on NAD+ metabolism and compared with administering no composition at all. In the one place the patent discusses the effect of the combination product on NAD+ metabolism, it is "optimized" relative to the effectiveness of an NR composition that is *not* in combination with tryptophan, nicotinic acid, or nicotinamide. '807 patent, 29:11-23; *see supra*, at 92.

F. "pharmaceutical composition"

TERM (PATENT/CLAIMS)	CHROMADEX'S PROPOSED CONSTRUCTION	ELYSIUM'S PROPOSED CONSTRUCTION
"pharmaceutical composition" ('086 patent, cl. 2)	This term should be construed according to its plain and ordinary meaning, but if construction is necessary, it should be construed as: "a composition suitable for ingestion by humans or other animals"	"A composition, including a food composition, that can be used to treat or prevent a disease or condition in humans or other animals."

1. ChromaDex's Opening Position

The term "pharmaceutical composition" as recited in claim 2 of the '086 patent has a plain and ordinary meaning and would be readily understood by a POSA. If the Court finds that construction is necessary, it should construe the term to mean "a composition suitable for ingestion by humans or other animals." *See Shire ViroPharma Inc. v. CSL Behring LLC*, C.A. No. 17-414, 2019 WL 6118253, at *12 (D. Del. Nov. 18, 2019) (construing "pharmaceutical composition" to mean "a composition for administration to a subject").

The parties agree that the recited "pharmaceutical composition" does not need to be a drug, but instead can take other forms, including food. The parties also agree that the recited "pharmaceutical composition" must be suitable for ingestion by

either humans or other animals. The only dispute is whether, as Elysium argues, the Court should import into claim 2 an embodiment that the recited pharmaceutical composition "can be used to treat or prevent a disease or condition."

Although the specification discloses certain exemplary embodiments in which the inventive compositions can be used to prevent or treat a disease or condition, it also discloses that NR-containing compositions can be used for other purposes. For example, the specification teaches that the inventive compositions can take the form of "a dietary supplement," '807 patent, 4:21-23, and can be used for "prolonging health and well-being," *id.*, 28:35-41. The specification similarly discloses that NR can be used to increase NAD+ biosynthesis independent of treating or preventing a particular disease or condition. *See, e.g.*, *id.*, 3:3-11; 28:35-41.

As these disclosures illustrate, there are potential uses of the inventive compositions other than preventing or treating a disease or condition. Moreover, there is no indication in the intrinsic evidence, let alone a "clear indication," that claim 2 should be *limited* to preventing or treating a disease or condition. *Liebel-Flarsheim*, 358 F.3d at 913. The Court should therefore reject Elysium's proposal to rewrite claim 2 to include that requirement. *See SuperGuide Corp. v. DirecTV Enterprises, Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004) ("[A] particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment.").

2. Elysium's Answering Position

"Pharmaceutical composition" appears in claim 1 of the '086 patent, from which asserted claim 2 depends. It is undisputed that the term is limiting, but the parties disagree on how it should be construed. It should be construed as "a composition, including a food composition, that can be used to treat or prevent a disease or condition in humans or other animals."[36]

The specification teaches that "***the present invention*** is a method for ***preventing or treating a disease or condition*** associated with the nicotinamide riboside kinase pathway of NAD+ biosynthesis." '086 patent at 4:17-19 (emphases added). "When a patent… describes the features of the 'present invention' as a whole, this description limits the scope of the invention." *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1308 (Fed. Cir. 2007). The specification further states that

> A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the effective amount of the pharmaceutical composition required ***for prevention or treatment*** in an animal subject….

'086 Patent at 31:42-45.

[36] Construction is necessary to determine, for example, whether the patent enables and describes the claimed invention over the full breadth of the claims.

Elysium's construction comports with the plain and ordinary meaning of "pharmaceutical composition." *See, e.g, Abbott Labs. v. Sandoz*, 529 F. Supp. 2d 893, 903 (N.D. Ill. 2007) (plain and ordinary meaning of "pharmaceutical composition" is "an aggregated product formed from two or more substances for use as a drug in medical treatment").[37]

By contrast, Plaintiffs' construction writes the word "pharmaceutical" out of the claims. Plaintiffs' construction requires only that the composition be "suitable for ingestion by humans or other animals." But claim 1 ***already*** requires that the composition be "formulated for oral administration." The "pharmaceutical" limitation would be meaningless under Plaintiffs' construction: "pharmaceutical composition" would have the same meaning as "composition."

Unlike the '086 patent, claims of the '807 patent are directed to "compositions" generally. Where the patentee claimed "pharmaceutical compositions" in one patent and more broadly claimed "compositions" in the other, the two terms should not be construed to have the same scope.

[37] Plaintiffs' reliance on *Shire ViroPharma, Inc. v. CSL Behring LLC*, 2019 U.S. Dist. LEXIS 198992 (D. Del. Nov. 18, 2019) is misplaced. In *Shire*, the dispute concerned whether the composition was limited to a liquid form. There was no reason for the court to reach the issue as to whether a pharmaceutical composition required that the composition be for treatment of a disease or condition.

3. ChromaDex's Reply Position

The plain and ordinary meaning of this term is "a composition suitable for ingestion by humans or other animals," and the intrinsic evidence does not support Elysium's proposed requirement that the recited pharmaceutical composition "can be used to treat or prevent a disease or condition."

It is immaterial that the specification discloses that "the present invention is a method for preventing or treating a disease or condition associated with the nicotinamide riboside kinase pathway of NAD+ biosynthesis." '086 patent, 4:17-19. It is well-established that a single patent specification can support several patents claiming different inventions, and that in any one patent the patentee "need not claim all that he is entitled to claim." *Application of Eickmeyer*, 602 F.2d 974, 981 (C.C.P.A. 1979). Here, unlike the claims of the related '832 application, which claimed "[a] method for preventing or treating a disease or condition associated with the nicotinamide riboside kinase pathway of NAD+ biosynthesis," Ex. 35 at 2, the claims of the '086 patent do not claim a method, but instead claim "pharmaceutical composition[s]." Thus, the specification's description of "a method for preventing or treating a disease or condition associated with the nicotinamide riboside kinase pathway of NAD+ biosynthesis" does not limit the claims of the '086 patent.

Notably, the specification also discloses that "the present invention is a dietary supplement composition," '086 patent, 4:14-16, and that the inventive compositions

can be used for "prolonging health and well-being," *id.*, 27:60-66, and increasing NAD+ biosynthesis independent of treating or preventing a particular disease or condition, *e.g.*, *id.*, 2:62-33, 27:60-66. In light of these disclosures that the inventive compositions have uses in addition to preventing or treating a disease or condition, and absent any indication that the embodiment of preventing or treating a disease or condition should be read into claim 2, Elysium's proposed construction is inconsistent with the intrinsic evidence. *See Liebel-Flarsheim*, 358 F.3d at 913; *SuperGuide*, 358 F.3d at 875.

Finally, Elysium is incorrect that "Plaintiffs' construction writes the word 'pharmaceutical' out of the claims." ChromaDex's proposed construction (if construction is necessary) is "a composition suitable for ingestion by humans or other animals," which relates to the safety of ingesting the pharmaceutical composition. By contrast, the limitation in claim 1 that the composition is "formulated for oral administration" relates to the form of the composition.

4. Elysium's Sur-Reply Position

Plaintiffs agree that "pharmaceutical composition" must mean more than "composition." But their argument that this term merely requires a composition that is "safe[]" to "ingest" (*supra*), ignores that pharmaceutical compositions must not only be safe but efficacious. A proper construction would require that the

composition treat or prevent a disease or condition in humans or other animals.[38] '086 patent, 4:17-19; 31:42-46.

Plaintiffs assert, without support, that their construction comports with the plain and ordinary meaning of "pharmaceutical composition." Dartmouth—once again—sang a different tune in the IPR proceedings. There, Dartmouth proffered an expert who testified that "what pharmaceutical means" is "has therapeutic or preventative effect." Ex. 40 at 19. In his IPR declaration, Dartmouth's expert wrote that a "POSITA understands that a pharmaceutical composition relates to medicinal drugs." Ex. 41 at ¶ 30.

Plaintiffs argue that a specification "can support several patents claiming different inventions." *Supra*, at 99. True, but this only makes Elysium's point. The '086 patent claims "pharmaceutical compositions" while the '807 patent claims "compositions." The terms are different, and by choosing "pharmaceutical composition" in claim 1, the applicant conveyed its intent in this application to claim a narrower invention, in which the composition treated or prevented a disease or condition in humans or other animals, as described in the specification. '086 patent, 4:17-19; 31:42-46.

[38] Plaintiffs do not dispute that the claim must be construed to encompass both humans and animals.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I, Adam W. Poff, hereby certify that on November 12, 2020, I caused to be electronically filed a true and correct copy of the foregoing document with the Clerk of the Court using CM/ECF, which will send notification that such filing is available for viewing and downloading to the following counsel of record:

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I further certify that on November 12, 2020, I caused the foregoing document to be served via electronic mail upon the above-listed counsel.

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