

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

CHROMADEX, INC. and
TRUSTEES OF DARTMOUTH
COLLEGE,

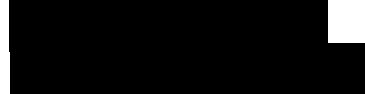
Plaintiffs,

v.

ELYSIUM HEALTH, INC.,

Defendant.

Civil Action No. 18-1434-CFC



**PLAINTIFFS' REPLY BRIEF IN SUPPORT OF THEIR
MOTION FOR SUMMARY JUDGMENT OF NO ANTICIPATION
OF U.S. PATENT NOS. 8,197,807 AND 8,383,086 (MOTION NO. 2) (D.I. 199)**

Dated: May 21, 2021

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Abbreviation	Description
The '807 Patent	U.S. Patent No. 8,197,807
The '086 Patent	U.S. Patent No. 8,383,086
Plaintiffs	collectively, Plaintiffs ChromaDex, Inc. and Trustees of Dartmouth College
Elysium	Defendant Elysium Health, Inc.
NR	nicotinamide riboside
isolated NR	isolated nicotinamide riboside
POSA	person of ordinary skill in the art
Goldberger I	Joseph Goldberger, et al., <i>A Study of the Blacktongue-Preventative Action of 16 Foodstuffs with Special Reference to the Identity of Blacktongue of Dogs and Pellagra</i> , Public Health Reports, vol. 43, pp. 1385-1455 (Jun. 8, 1928) [Ex. 3]
Goldberger II	Joseph Goldberger and W.F. Tanner, <i>A Study of the Treatment and Prevention of Pellagra</i> , Public Health Reports, vol. 39, pp. 1385-1455, (Jan. 18, 1924) [Ex. 4]
Holdsworth	Holdsworth, E. S., et al., "A Fraction Derived From Brewer's Yeast Inhibits Cholesterol Synthesis by Rat Liver Preparations in Vitro," <i>British Journal of Nutrition</i> 65.2 (1991): 285-299 [Ex. 5]
Trammell I	Trammell, Samuel AJ, et al., "Nicotinamide Riboside Is A Major NAD ⁺ Precursor Vitamin in Cow Milk," <i>The Journal of Nutrition</i> 146.5 (2016): 957-963 [Ex. 9]
D.I. 152	Claim Construction Order, No. 18-1434-CFC, D.I. 152 (Jan. 5, 2021)

D.I. 202	Opening Brief in Support of Plaintiffs' Motion for Summary Judgment of No Anticipation of U.S. Patent Nos. 8,197,807 and 8,383,086 (Motion No. 2), D.I. 202 (Apr. 27, 2021)
D.I. 272	Elysium's Answering Brief in Opposition to Plaintiffs' Motion for Summary Judgment of No Anticipation of U.S. Patent Nos. 8,197,807 and 8,383,086 (Motion No. 2), D.I. 272 (May 14, 2021)
Ex.	Exhibit of Declaration of Adam W. Poff in Support of Plaintiffs' Motion for Summary Judgment of No Anticipation of U.S. Patent Nos. 8,197,807 and 8,383,086 (Motion No. 2) (D.I. 222)
CSUF	Plaintiffs' Concise Statement of Undisputed Facts in Support of Plaintiffs' Motion for Summary Judgment of No Anticipation of U.S. Patent Nos. 8,197,807 and 8,383,086 (Motion No. 2), D.I. 201 (Apr. 27, 2021)
CSUF-Resp	Table 1, Elysium's Responses to Plaintiffs' CSUF, in Defendant Elysium Health, Inc.'s Counterstatement of Facts in Opposition to Plaintiffs' Concise Statement of Undisputed Facts in Support of Plaintiffs' Motion for Summary Judgment of No Anticipation of U.S. Patent Nos. 8,197,807 and 8,383,086 (Motion No. 2), D.I. 273 (May 14, 2021)
DCMF	Table 2, Defendant's Counterstatement of Material Facts, in Defendant Elysium Health, Inc.'s Counterstatement of Facts in Opposition to Plaintiffs' Concise Statement of Undisputed Facts in Support of Plaintiffs' Motion for Summary Judgment of No Anticipation of U.S. Patent Nos. 8,197,807 and 8,383,086 (Motion No. 2), D.I. 273 (May 14, 2021)

Elysium has no meaningful response to the simple and undisputed facts underlying Plaintiffs' motion. First, with regard to "isolated NR," this Court made clear at the *Markman* hearing that whether NR is "isolated" depends on whether the NR is "substantially free" of the other components associated with its source. Ex. 15, 29:13-22. The undisputed evidence (Trammell I) demonstrates that skimming milk reduces the concentration of NR—the opposite of isolation. That same uncontroverted evidence shows that skim milk contains only trace amounts of NR, confirming that skimming does not render the NR substantially free of the other components associated with its source. For buttermilk, no record evidence discloses either the effect of removing butter on milk's NR concentration or even what buttermilk's NR concentration is. Elysium thus cannot show that either processing method isolates the NR in milk.

Second, as to yeast, Elysium does not dispute that Holdsworth fails to describe both the contents of the yeast fraction ("N1") Elysium asserts contains isolated NR and the fraction's suitability for oral administration. Elysium thus cannot show that fraction N1 is an oral composition containing isolated NR in combination with a carrier.

Unable to dispute these dispositive facts, Elysium instead distracts with irrelevancies. For example, Elysium disputes direct quotes from the specification (CSUF-Resp-6), Elysium's website (CSUF-Resp-4), Trammell I (CSUF-Resp-9),

and Dr. Adams' deposition transcript (CSUF-Resp-22). Indeed, Elysium's counterstatement often cites evidence unrelated to Plaintiffs' original facts. *E.g.*, CSUF-Resp-10; CSUF-Resp-16. But Elysium's purported disputes are beside the point; the material facts are undisputed and confirm that Elysium cannot meet its burden to prove anticipation.¹

I. The NR in Skim Milk Is Not Isolated.

Skimming milk results in “no significant difference between the concentration of NR in skim milk and the concentration of NR in whole milk.” Ex. 7, ¶¶ 60-61, 87-88. Indeed, Elysium relies on this fact to oppose Plaintiffs' motion. DCMF-10. But the NR in skim milk cannot be “separated or substantially free from at least some of the other components associated with the source of the nicotinamide riboside,” and thus cannot be “isolated NR,” when skimming does not increase the ratio of NR to those other components.

Elysium illustrates its error with a hypothetical: removing “everything but NR from a gallon of milk” then adding two gallons of water. D.I. 272, 11. In this example, before the addition of water the NR is 100% pure—clearly substantially free of other components. The hypothetical demonstrates an isolation of NR

¹ Dr. Adams opined, “The Asserted Claims Are Anticipated And Obvious.” Ex. 6, § VIII. Claim 2 of the '086 Patent is an Asserted Claim, Ex. 6, ¶ 130, but Dr. Adams has offered no evidence or analysis to support anticipation of that claim. Summary judgment of no anticipation of the '086 Patent is thus warranted. *Vectura Ltd. v. GlaxoSmithKline LLC*, No. 16-638-RGA, 2019 WL 1244942, at *3-*4 (D. Del. Mar. 18, 2019).

(followed by dissolution). By contrast, skimming milk does not substantially free NR from other components and is not an isolation process. D.I. 202, 6-7.

The remainder of Elysium's response is inapposite. Elysium "disputes" Dr. Sobol's calculation of skim milk's NR concentration (0.000059%) because (1) Dr. Adams characterized the NR as "significant and biologically relevant," D.I. 272, 12, and (2) Trammell I reports skim milk's NR concentration as a range (3.1±1.6 μmol/L), indicating some "variance," CSUF-Resp-2(c). But Dr. Adams himself acknowledged that skimming has no significant effect on milk's NR concentration and never disputed Dr. Sobol's calculations. Ex. 10, 129:2-18, 131:9-20. These concessions confirm that skimming is not an isolation.

Elysium also alleges that Plaintiffs improperly require "isolated NR" to comprise either 25% or 0.1% NR. D.I. 272, 9-10. This is false—Plaintiffs do not reprise previous claim construction arguments. Plaintiffs cite the specification's guidance about the concentration of isolated polypeptides ("at least 25%") and active compounds for oral administration ("at least 0.1%") simply to contrast skim milk's low ratio of NR to other components (0.000059%). D.I. 202, 5-6. The orders-of-magnitude difference confirms skim milk's NR is not substantially free of other components. Whether it is "significant and biologically relevant" is not the issue; the NR must be isolated.

Elysium asserts Plaintiffs made a “stunning admission” that granting this motion requires choosing between “competing expert testimony.” D.I. 272, 1. This is deliberately misleading. Plaintiffs’ brief cites this Court’s observation that whether the “isolated NR” limitation is met depends on expert testimony about whether the NR is “substantially free” of other components.² D.I. 202, 9 (citing Ex. 15, 29:13-22). As Plaintiffs pointed out, Elysium did not (and could not) present such evidence. There is thus no competing expert testimony on the relevant question.

II. The NR in Buttermilk Is Not Isolated.

Elysium has adduced no evidence concerning either the effect of removing butter on the NR concentration in milk, or even what the NR concentration in buttermilk is. Dr. Adams testified he has never “seen any data on how much NR is in buttermilk.” CSUF-16. Without that, Elysium cannot prove the buttermilk of Goldberger II contains NR that is “separated or substantially free from at least some of the other components associated with the source of the nicotinamide riboside,” and thus, cannot prove anticipation by Goldberger II. *See Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc.*, 725 F.3d 1341, 1352 (Fed. Cir. 2013).

Elysium simply asserts that buttermilk contains some NR. D.I. 272, 13-14. The mere presence of NR, however, is insufficient to prove that it is “isolated.” D.I.

² Elysium’s anticipation argument relies on an improper, disjunctive interpretation of the Court’s construction that reads out the phrase “substantially free.” D.I. 272, 11-12.

152, 2. Moreover, Elysium’s only support for the presence of NR in buttermilk is a one-word deposition response from Dr. Sobol and Dr. Adams’ unsupported assertion. DCMF-15. Elysium does not account for the record evidence showing that processing milk may lead to a reduction in the NR concentration. *See* CSUF-13; CSUF-14. The record evidence therefore supports nothing more than a possibility—insufficient for anticipation—that some NR survives the process of making buttermilk. *MEHL/Biophile Int’l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999).

III. The Yeast Fraction in Holdsworth Is Not an Oral Composition of Isolated NR in Admixture with a Carrier.

Elysium maintains that Holdsworth discloses isolated NR “in brewer’s yeast *fractions*, meaning they are separated from at least some of the components of the original yeast.” D.I. 272, 16. But Elysium erroneously conflates those “fractions” with yeast itself and fails to adduce evidence that any fraction is an oral composition comprising isolated NR in admixture with a carrier, as the claims require.

Elysium points to yeast fraction N1 as a composition containing isolated NR. *Id.*, 6, 15. Holdsworth never describes N1 (or any other fraction) as a composition for oral administration; indeed, a POSA would understand the fractionation method (extraction with ammonia followed by chromatography) as contradicting such a

conclusion.³ D.I. 202, 12. While Elysium asserts that “Holdsworth teaches oral compositions containing yeast,” D.I. 272, 15, that is irrelevant. Elysium argues it is a fraction, not the yeast, that contains the isolated NR, but identifies nothing in Holdsworth that describes N1 (or any fraction) as an oral composition.

Moreover, Elysium fails to address Plaintiffs’ showing that no fraction comprises a carrier. *Id.*, 15. Elysium points to Dr. Adams’ testimony that yeast cells contain “sugars,” *id.*, 16, but Elysium identifies no evidence that any fraction contains a sugar. *See* Ex. 10, 143:15-144:2.

Finally, as with buttermilk, there is no evidence of the composition or NR concentration of fraction N1 (or even yeast). Ex. 10, 139:4-140:23, 143:15-144:2. Elysium cannot prove that Holdsworth describes isolated NR without this evidence.

³ Elysium asserts that ammonia might not render a yeast fraction unsuitable for oral administration, D.I. 272, 15-16, but points to no expert testimony describing N1 as suitable for oral administration. “[A]ttorney argument d[oes] not demonstrate a genuine issue of material fact.” *Taurus IP, LLC v. DaimlerChrysler Corp.*, 726 F.3d 1306, 1324-25 (Fed. Cir. 2013).

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WORD COUNT CERTIFICATION

The undersigned counsel hereby certifies that the foregoing brief complies with the type-volume limitations of paragraph 20(c) of the Scheduling Order (D.I. 40). The text of the brief, including footnotes, was prepared using Times New Roman 14-point font, and it contains 1326 words (excluding the title, caption, tables, and signature block).

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