

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

CHROMADEX, INC. and
TRUSTEES OF DARTMOUTH
COLLEGE,

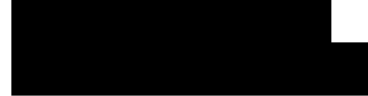
Plaintiffs,

v.

ELYSIUM HEALTH, INC.,

Defendant.

Civil Action No. 18-1434-CFC



**PLAINTIFFS' RESPONSE TO ELYSIUM'S MOTION FOR
SUMMARY JUDGMENT (NO. 1) OF INVALIDITY
UNDER 35 U.S.C. § 101 (D.I. 183)**

Dated: May 14, 2021

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TABLE OF CONTENTS

TABLE OF AUTHORITIES ii

TABLE OF ABBREVIATIONS iii

ARGUMENT 2

I. *Alice* Step One: The Asserted Claims Are Directed to Patent Eligible
Concepts. 2

 A. Elysium’s Focus on Milk Is Misguided. 2

 B. The Claimed Compositions Have Different Characteristics
 Than, and the Potential for Significant Utility Beyond, Milk..... 4

 1. The Claimed Compositions Have Very Different
 Characteristics Than Naturally Occurring NR..... 4

 2. The Compositions of the Asserted Claims Can Be Used
 Differently Than NR in Nature. 6

II. *Alice* Step Two: Dartmouth’s Claims Disclose an Inventive Concept..... 8

CONCLUSION 11

TABLE OF AUTHORITIES

	Page(s)
Cases	
<i>Alice Corp. Pty. v. CLS Bank Int’l</i> , 573 U.S. 208 (2014).....	2, 9, 10
<i>Ass’n for Molecular Pathology v. Myriad Genetics, Inc.</i> , 569 U.S. 576 (2013).....	3
<i>In re Bhagat</i> , 726 F. App’x 772 (Fed. Cir. 2018).....	3
<i>BRCA1 & BRCA2-Based Hereditary Cancer Test Patent Litig. v. Ambry Genetics Corp.</i> , 774 F.3d 755 (Fed. Cir. 2014)	3
<i>Diamond v. Chakrabarty</i> , 447 U.S. 303 (1980).....	1, 3, 9
<i>Diamond v. Diehr</i> , 450 U.S. 175 (1981).....	10
<i>Funk Bros. Seed Co. v. Kalo Inoculant Co.</i> , 333 U.S. 127 (1948).....	3, 4
<i>Genetic Techs. Ltd. v. Merial L.L.C.</i> , 818 F.3d 1369 (Fed. Cir. 2016)	10
<i>Mayo Collaborative Servs. v. Prometheus Labs., Inc.</i> , 566 U.S. 66 (2012).....	2, 9
<i>Nat. Alternatives Int’l, Inc. v. Creative Compounds, LLC</i> , 918 F.3d 1338 (Fed. Cir. 2019)	1, 3, 7, 8
<i>Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.</i> , 827 F.3d 1042 (Fed. Cir. 2016)	2, 11
Statutes	
35 U.S.C. § 101	1, 2, 11, 12

TABLE OF ABBREVIATIONS

Abbreviation	Description
The Dartmouth Patents	U.S. Patent Nos. 8,383,086 and 8,197,807
The '807 Patent	U.S. Patent No. 8,197,807
The '086 Patent	U.S. Patent No. 8,383,086
The Asserted Claims	Claims 1-3 of the '807 Patent and Claim 2 of the '086 Patent
ChromaDex	Plaintiff ChromaDex, Inc.
Dartmouth	Plaintiff Trustees of Dartmouth College
Plaintiffs	collectively, Plaintiffs ChromaDex, Inc. and Trustees of Dartmouth College
Elysium	Defendant Elysium Health, Inc.
NR	nicotinamide riboside
isolated NR	isolated nicotinamide riboside
D.I. 183	Elysium's Opening Brief in Support of Motion for Summary Judgment (No. 1) of Invalidity Under 35 U.S.C. § 101
D.I. 184	Elysium's Statement of Facts in Support of Its Motion for Summary Judgment (No. 1) of Invalidity Under 35 U.S.C. § 101
XSF	Plaintiffs' Response & Concise Counterstatement of Facts in Opposition to Elysium's Motion for Summary Judgment (No. 1) of Invalidity Under 35 U.S.C. § 101
Ex.	Exhibit to Declaration of Adam W. Poff in Support of Plaintiffs' Response to Elysium's Motion for Summary Judgment (No. 1) of Invalidity Under 35 U.S.C. § 101

The Court should deny Elysium’s motion for summary judgment of invalidity under 35 U.S.C. § 101. To warrant summary judgment of invalidity, a movant must show that there exists no genuine dispute of material facts, such that the undisputed facts clearly and convincingly establish patent invalidity. Elysium does not, and cannot, meet this heavy burden.

The Federal Circuit directly addressed the patentability of compositions of naturally-occurring compounds in *Nat. Alternatives Int’l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338 (Fed. Cir. 2019). The Court upheld their patentability, holding that “[a] claim to a manufacture or composition of matter made from a natural product is not directed to the natural product where it has different characteristics and ‘the potential for significant utility.’” *Id.* at 1348 (quoting *Diamond v. Chakrabarty*, 447 U.S. 303, 310 (1980)).

Elysium never addresses this test, and D.I. 184 does not even attempt to adduce undisputed evidence that the claimed compositions have neither different characteristics nor the potential for significant utility compared to NR as found in nature. Nor could Elysium, as there is substantial evidence that the claimed compositions are significantly different from milk. Elysium’s motion should be denied.

ARGUMENT

Determining patent eligibility under 35 U.S.C. § 101 requires a two-step inquiry. *See Alice Corp. Pty. v. CLS Bank Int’l*, 573 U.S. 208, 217-18 (2014). “Step one asks whether the claim is directed to one of the patent-ineligible concepts. If the answer is no, the inquiry is over: the claim falls within the ambit of § 101.” *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042, 1047 (Fed. Cir. 2016) (citations and internal quotations omitted). Only if the claim fails step one does the inquiry move to step two, “which asks whether, considered both individually and as an ordered combination, the additional elements transform the nature of the claim into a patent-eligible application.” *Id.* (internal quotations omitted).

To succeed, Elysium must prove clearly and convincingly that the Asserted Claims fail both steps and that there exists no genuine dispute of material facts. Elysium does neither.

I. *Alice* Step One: The Asserted Claims Are Directed to Patent Eligible Concepts.

A. Elysium’s Focus on Milk Is Misguided.

Because “NR is a naturally-occurring vitamin present in cow milk,” Elysium argues, the claimed compositions containing isolated NR are directed to unpatentable products of nature. D.I. 183 at 1, 4-5. But the mere fact that NR is found in nature does not establish that the claimed compositions are directed to patent-ineligible subject matter. Instead, Elysium must show that those compositions do not

“ha[ve] different characteristics and the potential for significant utility” beyond NR found in nature. *Nat. Alternatives*, 918 F.3d at 1348 (internal quotation omitted).

The case law cited by Elysium confirms this requirement. See *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 593 (2013) (explaining isolation in claims was not relevant to patent eligibility because there were no “changes that result[ed] from the isolation”); *In re Bhagat*, 726 F. App’x 772, 779 (Fed. Cir. 2018) (finding claims ineligible because there was no “transformation” of the natural product nor did the claims “have properties not possessed by these products in nature”); *BRCA1 & BRCA2-Based Hereditary Cancer Test Patent Litig. v. Ambry Genetics Corp.*, 774 F.3d 755, 760 (Fed. Cir. 2014) (quoting *Diamond*, 447 U.S. at 310) (claims are ineligible where they do not possess “markedly different characteristics from [anything] found in nature”); *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948) (holding claims ineligible where the claimed combination of bacteria species provided “no enlargement of the range of their utility” and “d[id] not improve in any way their natural function.”)

The correct inquiry under *Alice* step 1 is thus whether compositions of the Asserted Claims “have different characteristics and can be used in a manner that [NR] as it appears in nature cannot.” *Nat. Alternatives*, 918 F.3d at 1348. D.I. 184 never puts forth facts addressing this inquiry. At most, Elysium avers that milk can be used to treat pellagra and black-tongue, disorders associated with deficiencies in

NAD⁺ biosynthesis. D.I. 184 ¶¶ 7-9. This is far from sufficient to establish that the claimed compositions lack distinguishing characteristics or significant utility compared to milk.

There is substantial evidence that the claimed compositions of isolated NR have characteristics and utility dramatically different from milk. Moreover, Elysium has the inquiry backwards. That milk may have some utility of its own does not mean that the claimed compositions comprising isolated NR lack the potential for significant utility beyond milk. D.I. 184 does not address this question, let alone aver that the claimed compositions lack any significant utility beyond milk. Elysium's motion thus fails even to attempt the showing required to establish that claims to formulations of naturally-occurring nutrients are directed to patent-ineligible subject matter. This alone warrants denial of the motion.

B. The Claimed Compositions Have Different Characteristics Than, and the Potential for Significant Utility Beyond, Milk.

Moreover, there are ample facts showing that the claimed compositions have different characteristics than, and the potential for significant utility beyond, milk.

1. The Claimed Compositions Have Very Different Characteristics Than Naturally Occurring NR.

The use of isolated NR in the Asserted Claims requires that the NR in the claimed compositions be stable and bioavailable, allowing it to reach the bloodstream, enter the cell, and provide therapeutic effect. *See, e.g.*, XSF-14; Ex. 1,

¶¶ 142, 144, 154, 157. That is not true of NR as it is found in nature. First, the NR in milk is present in only trace amounts—around 1 part per million—three orders of magnitude less than the minimum taught in the patent for achieving effective use, and far too little to exert any therapeutic effect. XSF-14; Ex. 1, ¶¶ 73-75, 88, 152-154; Ex. 2, 128:19-129:11; Ex. 3, 30:23-29. Elysium itself touts the fact that “[w]hile NR and NMN can be found in trace amounts in various foods, though, one cannot eat enough of anything to boost NAD⁺ levels.” XSF-14; Ex. 4, 000165405; *see also* Ex. 5, 000165201 (Observer article, Aug. 27, 2017) (“Unlike the vast majority of vitamins and dietary supplements ... the molecules in Basis have been demonstrated to be bioavailable, meaning they get into the body and do what they’re intended to, including raising NAD⁺ levels.”).

The NR in milk is neither bioavailable nor stable. Indeed, the very literature Elysium cites for the presence of NR in milk—D.I. 183, Ex. L (“Trammell I”)—teaches that the minuscule amounts of NR in milk is bound to the lactalbumin whey protein. As Elysium’s expert conceded, Trammell I teaches that the lactalbumin “binds NR and keeps it bound to the protein so that it is not biologically available when you drink milk.” XSF-14; Ex. 2, 120:2-8; Ex. 1, ¶ 332. He further acknowledged that even were NR free in the “water fraction” of the milk, it would be subject to degradation through hydrolysis and thus equally unavailable. XSF-14; Ex. 2, 122:13-20.

The characteristics of the claimed compositions dramatically distinguish those compositions from naturally occurring NR. The claimed compositions contain isolated NR that is stable, bioavailable, and sufficiently pure that the compositions can be administered orally to deliver NR to the cells of an animal and exert therapeutic effect. Elysium’s motion contains no showing that the NR in milk even reaches the bloodstream after the milk is consumed, let alone enters cells and provides therapeutic effect. While Elysium points to the therapeutic effect of milk in treating pellagra and black-tongue, it is widely accepted that that effect results from the tryptophan in milk, not the NR. XSF-14; Ex. 1, ¶¶ 296-301. Entirely absent from Elysium’s motion is any evidence showing that naturally occurring NR is stable, bioavailable, and capable of achieving therapeutic effect. The isolated NR of the claimed compositions is all three.¹

2. The Compositions of the Asserted Claims Can Be Used Differently Than NR in Nature.

The compositions in the Asserted Claims “can be used in a manner that [NR] as it appears in nature cannot.” *Nat. Alternatives*, 918 F.3d at 1348. Because the NR in the claimed compositions is isolated—and therefore stable, bioavailable, and

¹ Elysium argues that the claimed compositions of the ’807 Patent require only that the composition as a whole increase NAD⁺ biosynthesis and not just the NR. This misses the point. The compositions of the ’807 Patent contain isolated NR, and it is this isolated NR that is stable and bioavailable, giving the claimed compositions the potential for utility far beyond milk. Though both tryptophan in milk and NR in the claimed compositions may be capable of treating pellagra, they act through different pathways and achieve different biological effects.

pure—the claimed compositions can be used to deliver effective amounts of NR to cells. Indeed, isolated NR has proved to be uniquely effective. XSF-14; Ex. 1, ¶¶ 954-55. The effects of the claimed compositions go far beyond the treatment of pellagra or black-tongue. The unique ability of isolated NR to enhance NAD⁺ biosynthesis allows the claimed compositions to enhance cellular health well beyond anything that can be achieved with milk. *See* XSF-14; Ex. 1, ¶¶ 973-976. Elysium itself has filed patent applications for the use of compositions of isolated NR to treat a wide variety of disorders, including kidney disease, premature aging, and neurodegenerative diseases. *See* XSF-14; Ex. 1, ¶¶ 67-69. This exceeds anything milk can achieve.

Elysium argues that the “claims do not specify a minimum quantity of NR that must be present in the composition, let alone a quantity ‘far beyond that found in nature.’” D.I. 183 at 13. First, regardless of amount, the isolated NR of the Asserted Claims is stable and bioavailable—a significant distinction from the NR in milk. The claimed compositions can be used to deliver NR to the bloodstream and thereby activate the NR pathway; milk cannot. This gives the claimed compositions the potential for utility milk simply does not have.

Second, the claims do require that the compositions have the capability to improve health and well-being (the ’086 Patent) or enhance NAD⁺ biosynthesis (the ’807 Patent). *See* D.I. 152. The patent teaches that the claimed compositions contain

at least 0.1% isolated NR to achieve these effects. XSF-14; Ex. 3, 30:23-29. This is a thousand times more than the NR in milk. *See supra* p. 5.

Regardless, Elysium's focus on the amount of isolated NR required by the Asserted Claims is irrelevant. Under controlling case law, the question is whether the claimed composition has "the potential for significant utility." *Nat. Alternatives*, 918 F.3d at 1348 (quoting *Diamond*, 447 U.S. at 310). The claimed compositions of isolated NR unquestionably have the potential for significant utility far beyond that of milk. To the extent that a given formulation contains less isolated NR, more of the formulation may have to be taken. But this is a stark contrast to milk, where the lack of isolation of the NR not only renders that NR both unstable and not bioavailable, but also prevents consumption of sufficient quantities to deliver effective amounts of NR at all. *See* XSF-14; Ex. 1, ¶ 75.

There is more than sufficient evidence upon which a factfinder could reasonably conclude that the claimed compositions have different characteristics than and the potential for significant utility beyond milk. As such, the claims are directed to patentable subject matter and Elysium's summary judgment motion should be denied.

II. *Alice* Step Two: The Asserted Claims Disclose an Inventive Concept.

Even if the Court were to conclude that one or more of the Asserted Claims were directed to patent-ineligible concepts, the claims nonetheless satisfy step two

of the *Alice/Mayo* test, requiring that the claims provide an “inventive concept” that “transform[s] the nature of the claim into a patent-eligible application.” *Alice*, 573 U.S. at 217 (internal quotation omitted).

As noted above, a wealth of evidence exists describing the benefits of the claimed compositions of the Dartmouth Patents over naturally occurring NR. This includes Elysium’s own representations. *See supra* p. 5. Elysium asserts that the “only alleged difference between the claims and natural whole milk is that the NR is ‘isolated,’” and that isolation is “well-understood, routine, and conventional activity.” D.I. 183 at 15. Elysium is incorrect. The claims are distinguished from the prior art in that isolated NR is formulated for oral administration. Achieving this required the inventive step of recognizing the utility of NR for enhancing health and well-being—a utility neither taught in the prior art nor even an inherent property of naturally-occurring NR, as the NR must be isolated and formulated for oral administration to achieve its effects. This recognition is absent from the prior art and a technological advance embodied in the claimed compositions.

Elysium’s reliance on *Genetic Techs. Ltd.* is misplaced. *See* D.I. 183 at 15-16. Elysium asserts that the Asserted Claims contain no inventive concept because the claims “cannot rely on the novelty of [the discovery of a patent-ineligible concept] for the inventive concept.” *Id.* This holding is inapposite. The inventive concept of the Asserted Claims is not the *discovery* of the NR vitamin pathway, but rather

therapeutic *applications* of this discovery in inventive ways beyond that of the prior art.

In *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, the Federal Circuit explained that a claim that “applies the discovery” to achieve something new and useful suffices to provide an inventive concept. 827 F.3d 1042, 1050-51 (Fed. Cir. 2016). The claimed compositions of isolated NR are undeniably new and useful. Further, that the individual steps of isolating a compound and formulating it “were known independently in the art does not make the claim unpatentable.” *Id.* at 1051. Here, prior art discloses neither the utility of isolated NR nor the concept of formulating it for oral administration. The claims thus embody both the recognition of the NR pathway and the further inventive concept that compositions of isolated NR could be orally administered to achieve new therapeutic effects—an insight well beyond anything then known or contemplated in the field. XSF-15; Ex. 1, ¶¶ 162-64. The claims thus encompass an inventive concept far beyond what was already known or contemplated in the field. As the Federal Circuit warned, “[t]o require something more at step two would be to discount the human ingenuity that comes from applying a natural discovery in a way that achieves a new and useful end.” *CellzDirect*, 827 F.3d at 1051-52 (internal quotation omitted). To the extent this Court reaches step 2 of the patent eligibility analysis, Elysium’s motion should be denied, as it has failed

to establish with undisputed facts that the Asserted Claims clearly lack an “inventive concept.”

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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 2,441 words (excluding the title, caption, tables, and signature block).

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CERTIFICATE OF SERVICE

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