Exhibit A

United States Court of Appeals for the Federal Circuit

CHROMADEX, INC., TRUSTEES OF DARTMOUTH COLLEGE,
Plaintiffs-Appellants

v.

ELYSIUM HEALTH, INC.,
Defendant-Appellee

2022-1116

Appeal from the United States District Court for the District of Delaware in No. 1:18-cv-01434-CFC-JLH, Chief Judge Colm F. Connolly.

Decided: February 13, 2023

WILLIAM L. MENTLIK, Lerner, David, Littenberg, Krumholz & Mentlik, LLP, Cranford, NJ, argued for plaintiffs-appellants. Also represented by RUSSELL W. FAEGENBURG, STEPHEN F. ROTH; ROBERT JASON FOWLER, CHRISTOPHER NEIL SIPES, ASHLEY MARIE WINKLER, Covington & Burling LLP, Washington, DC.

JEREMY YOUNKIN, Foley Hoag LLP, Boston, MA, argued for defendant-appellee. Also represented by DONALD ROSS WARE.

Before PROST, CHEN, and STOLL, *Circuit Judges*.

PROST, *Circuit Judge*.

ChromaDex, Inc. ("ChromaDex") and the Trustees of Dartmouth College ("Dartmouth") (collectively, "Appellants") appeal the decision of the U.S. District Court for the District of Delaware granting Elysium Health, Inc.'s ("Elysium") motion for summary judgment that the asserted claims of U.S. Patent No. 8,197,807 ("the '807 patent") are directed to unpatentable subject matter under 35 U.S.C. § 101.[1] We affirm.

BACKGROUND

I

The '807 patent is directed to dietary supplements containing isolated nicotinamide riboside ("NR"), a form of vitamin B3 naturally present—in non-isolated form—in cow's milk and other products.[2] *See* '807 patent col. 27 ll. 42–45. Animal cells convert ingested NR into the coenzyme nicotinamide adenine dinucleotide, or NAD+. NAD+ deficiencies can cause diseases in both animals and humans.

The asserted claims are claims 1–3 of the '807 patent. Representative claim 1 recites:

> 1. A composition comprising isolated nicotinamide riboside in combination with one or more of tryptophan, nicotinic acid, or nicotinamide, wherein said combination is in admixture with a carrier

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[1] Appellants also sought review of the district court's invalidation of claim 2 of U.S. Patent No. 8,383,086. The voluntary dismissal of a related appeal mooted that part of the case.

[2] For the sake of brevity, we use the word "milk" in the rest of this opinion to describe natural cow's milk.

> comprising a sugar, starch, cellulose, powdered tragacanth, malt, gelatin, talc, cocoa butter, suppository wax, oil, glycol, polyol, ester, agar, buffering agent, alginic acid, isotonic saline, Ringer's solution, ethyl alcohol, polyester, polycarbonate, or polyanhydride, wherein said composition is formulated for oral administration and increased NAD+ biosynthesis upon oral administration.

II

ChromaDex sells, among other products, dietary supplements in the form of pharmaceutical compositions of NR embodying the '807 patent. It licenses the patent from Dartmouth. Appellants sued Elysium, a former ChromaDex customer, for patent infringement in September 2018. The district court construed several claim terms; relevant here, the court construed "isolated [NR]" to mean "[NR] that is separated or substantially free from at least some other components associated with the source of [NR]." J.A. 22.

Elysium moved for summary judgment, arguing that the asserted claims were invalid under 35 U.S.C. § 101, and the district court granted the motion. *See ChromaDex, Inc. v. Elysium Health, Inc.*, 561 F. Supp. 3d 460 (D. Del. 2021). The district court concluded that the claims were directed to a natural phenomenon, namely, "compositions comprising isolated [NR], a naturally occurring vitamin present in cow milk." *Id.* at 464 (cleaned up). It rejected ChromaDex's argument that the characteristics of isolated NR purportedly different from naturally occurring NR—stability, bioavailability, sufficient purity, and therapeutic efficacy—render the claims patent-eligible, observing that none of those characteristics were part of the claims. *Id.* at 465. It concluded that "the decision to create an oral formulation of NR after discovering that NR is orally bioavailable is simply applying a patent-ineligible law of nature." *Id.* at 467.

The district court entered judgment of invalidity, and this appeal followed.[3] We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

I

We review the district court's grant of summary judgment under the law of the regional circuit, here the Third Circuit, which reviews such issues de novo. *Junker v. Med. Components, Inc.*, 25 F.4th 1027, 1032 (Fed. Cir. 2022) (citing *Gonzalez v. Sec'y of Dep't of Homeland Sec.*, 678 F.3d 254, 257 (3d Cir. 2012)). Summary judgment is appropriate when, drawing all reasonable inferences in the nonmoving party's favor, "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a); *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986). Eligibility under § 101 may involve questions of fact but is, ultimately, a question of law that we review de novo. *Nat. Alts. Int'l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338, 1342 (Fed. Cir. 2019); *Interval Licensing LLC v. AOL, Inc.*, 896 F.3d 1335, 1342 (Fed. Cir. 2018).

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a

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[3] Appellants also challenge the district court's orders granting-in-part Elysium's motion to dismiss for lack of standing and denying its motion for leave to amend, as well as one of its claim constructions. The district court's standing order only dismissed claims of infringement based on activities alleged to have occurred on or after March 13, 2017, *see* J.A. 16–17, so the eligibility issue remained live. Because we affirm the district court's invalidity judgment, we do not reach either the standing or the claim construction issues.

patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. "Laws of nature, natural phenomena, and abstract ideas," in contrast, "are not patentable." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 589 (2013).

II

The parties agree that NR is naturally present in milk. It is undisputed that milk is a naturally occurring product that is not patent eligible. The parties also acknowledge that milk contains tryptophan and lactose, a sugar. And no one disputes that the tryptophan in milk treats NAD+ deficiencies. The claims are very broad and read on milk with only one difference as shown:

Element	**Milk**
[1p] "A composition comprising"	Milk is a composition.
[1a] "isolated [NR]"	Milk contains NR, but the NR is not isolated. J.A. 10095.
[1b] "in combination with one or more of tryptophan, nicotinic acid, or nicotinamide"	Milk contains tryptophan and nicotinamide. J.A. 10095.
[1c] "wherein said combination is an admixture with a carrier comprising a sugar, starch, cellulose, powdered tragacanth, malt, gelatin, talc, cocoa butter, suppository wax, oil, glycol, polyol, ester, agar, buffering agent, alginic acid, isotonic	Milk is an admixture containing a sugar (lactose). J.A. 10096

saline, Ringer's solution, ethyl alcohol, polyester, polycarbonate, or polyanhydride"	
[1d] "wherein said composition is formulated for oral administration"	Milk is formulated for oral administration. *See* J.A. 10096.
[1e] "and increases NAD+ biosynthesis upon oral administration."	Milk (through tryptophan) increases NAD+ biosynthesis upon consumption. *See* J.A. 10096.

So the only difference between at least one embodiment within the scope of the claims and natural milk is that the NR in the former is isolated.

The Supreme Court's decisions in *Myriad* and *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980), apply here. In *Chakrabarty*, the Court found eligible claims to a genetically engineered bacterium "capable of breaking down multiple components of crude oil." 447 U.S. at 305, 318. No naturally occurring bacteria possessed the same property. *Id.* Accordingly, in the Court's view, the "claim [was] not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity having a distinctive name, character and use." *Id.* at 309–10 (cleaned up). Because "the patentee ha[d] produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility," the Court upheld the claims. *Id.* at 310.

As in *Myriad*, under the circumstances presented here, the act of isolating the NR compared to how NR naturally exists in milk is not sufficient, on its own, to confer patent eligibility. *See Myriad*, 569 U.S. at 590–93. The claimed compositions remain indistinguishable from natural milk

because, other than separation from some other components, the isolated NR is no different structurally or functionally from its natural counterpart in milk. *Chakrabarty* defines the inquiry: to be patentable, the claimed composition must "ha[ve] markedly different characteristics and have the potential for significant utility." 447 U.S. at 310. Milk, like the claimed compositions, undisputedly "increase[s] NAD+ biosynthesis" upon oral administration. The claimed compositions do not exhibit markedly different characteristics from natural milk and are, therefore, invalid for claiming a patent-ineligible product of nature. *Cf. Myriad*, 569 U.S. at 579 (concluding "that a naturally occurring DNA segment is *a product of nature* and not patent eligible merely because it has been isolated" (emphasis added)).

Our *Natural Alternatives* decision is particularly instructive. There, we upheld, at the motion-to-dismiss stage, claims directed to dietary supplements containing beta-alanine. *See* 918 F.3d at 1341. We concluded that the patents there claimed "specific treatment formulations that incorporate[d] natural products" and that those formulations "ha[d] different characteristics and c[ould] be used in a manner that beta-alanine as it appears in nature cannot." *Id.* at 1348. Specifically, the "natural products ha[d] been isolated and then incorporated into a dosage form"—"between about 0.4 grams to 16 grams"—"with particular characteristics"—namely, to "effectively increase[] athletic performance." *Id.* at 1348–49. Those markedly different characteristics distinguished the claimed supplements from natural beta-alanine and preserved the claims' validity. *Id.* at 1349.

Here, in contrast, the asserted claims do not have characteristics markedly different from milk. Both the claimed compositions and milk "increase[] NAD+ biosynthesis upon oral administration." Appellants argue that the claimed compositions are advantageous over milk because the isolation of NR allows for significantly more NAD+

biosynthesis than is found in milk and that the large quantity of NR itself *can alone* increase NAD+ biosynthesis. But the asserted claims do not require any minimum quantity of isolated NR. Nor do these claims attribute the claimed increase in NAD+ biosynthesis to the isolated NR, requiring only that the *composition* increase NAD+ production. Because milk increases NAD+ biosynthesis, the claimed compositions do not possess characteristics markedly different from those found in nature. To be sure, the claims cover several different composition embodiments, some of which are structurally different from milk. However, as noted above, the claims also encompass—as both parties agree—at least one embodiment that covers milk, except that the NR element is "isolated." Because the claims are broad enough to encompass a product of nature, it is invalid under § 101.

Appellants nonetheless argue that the claims, in fact, possess markedly different characteristics that render them patent-eligible. *See* Appellants' Br. 28–31. They base this argument on two main points: (1) "NR is found in milk in only trace amounts," *i.e.*, one part per million; and (2) "what little NR is found in milk is not bioavailable" because it is bound to the lactalbumin whey protein. *Id.* at 29.[4] The problem for Appellants is two-fold. First, as

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[4] Appellants also identify a factual error in the district court's opinion. The court stated that it was "undisputed that NR in milk . . . enhances NAD+ biosynthesis." *ChromaDex*, 561 F. Supp. 3d at 465. Appellants correctly point out that the NR in milk does not enhance NAD+ biosynthesis, that it argued as much to the district court, and that Elysium conceded the point. *See, e.g.*, J.A. 10245 (Elysium admitting that "one can't eat enough of anything [containing trace amounts of NR] to boost NAD+ levels"). That error was harmless, however, because the claims do not require that the NR, specifically, increase NAD+

discussed above, milk increases NAD+ biosynthesis (albeit because it contains tryptophan rather than because of the trace amounts of NR), and that is the only therapeutic effect that the claims require. Second, the claims simply do not reflect the distinctions Appellants rely on: they do not require any specific quantity of isolated NR, and the district court's construction for "isolated [NR]," which Appellants do not challenge on appeal, does not require that the NR be separated from the lactalbumin whey protein but only from "*some* of the other components associated with the source of [NR]." J.A. 22 (emphasis added). The claims, therefore, do not necessarily require that the isolated NR be bioavailable, meaning that the claimed compositions do not necessarily possess markedly different characteristics from milk, as they must to be patent-eligible.

We conclude that the asserted claims lack markedly different characteristics from milk. They claim a product of nature and are not patent eligible.

III

The inquiry could end here—the Supreme Court in *Myriad* relied on *Chakrabarty*'s "markedly different characteristics" framework for analyzing whether the claimed compositions there were directed to a natural phenomenon; the Court never applied the *Alice*/*Mayo* two-step framework despite deciding the case after *Mayo*. *See Myriad*, 569 U.S. at 593–95; *see also Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 217 (2014); *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 77–80 (2012). But if resort to *Alice*/*Mayo* is necessary, then at step one we conclude the asserted claims are directed to a product of nature for the reasons stated above, and at step two the claims lack an inventive step because they are directed to

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biosynthesis; it is enough if the claimed composition accomplishes that objective, and milk does so.

nothing more than compositions that increase NAD+ biosynthesis, which is the very natural principle that renders the claims patent-ineligible.[5]

Appellants identify only two possible inventive steps: "[1] recognizing the utility of NR for enhancing health and well-being and [2] the wisdom of *isolating* the NR to provide concentrations higher than what occur naturally." Appellants' Br. 31 (emphasis original). But recognizing the utility of NR is nothing more than recognizing a natural phenomenon, which is not inventive. *See Myriad*, 569 U.S. at 591. And the act of isolating the NR by itself, no matter how difficult or brilliant it may have been (although the specification makes clear that it was conventional), similarly does not turn an otherwise patent-ineligible product of nature into a patentable invention. *See id.* So the claims would likewise fail at step two.

CONCLUSION

We have considered Appellants' remaining arguments and find them unpersuasive. As Appellants conceded at oral argument, our resolution of the patent-eligibility issue moots the standing question. For the reasons set forth

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[5] In *Natural Alternatives*, we purported to analyze the patent-eligibility of the claimed compositions under *Alice*/*Mayo*'s two-step framework. *See Nat. Alts.*, 918 F.3d at 1342, 1348–49. But because we concluded that factual allegations relating to the claimed compositions' markedly different characteristics from natural beta-alanine precluded judgment on the pleadings, the analysis functionally examined only the *Chakrabarty* question. *See id.* at 1348. Indeed, in one prior case, we analyzed composition-of-matter claims under *Myriad* and *Chakrabarty* but analyzed method claims under *Mayo*. *Compare In re BRCA1- and BRCA2*, 774 F.3d 755, 759–61 (Fed. Cir. 2014), *with id.* at 761–765.

above, we affirm the district court's judgment that the asserted claims of the '807 patent are invalid under 35 U.S.C. § 101.

AFFIRMED