2019-1630

In The

United States Court Of Appeals

For The Federal Circuit

ELYSIUM HEALTH, INC.,

Appellant,

v.

TRUSTEES OF DARTMOUTH COLLEGE,

Appellee.

ON APPEAL FROM PATENT AND TRADEMARK OFFICE –
PATENT TRIAL AND APPEAL BOARD IN INTER PARTES REVIEW
NO. IPR2017-01795

REPLY BRIEF OF APPELLANT

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CERTIFICATE OF INTEREST

Counsel for Appellant Elysium Health, Inc. hereby certifies the following:

1. The full name of every party represented by me is:

Elysium Health, Inc.

2. The name of the real party in interest represented by me is:

Elysium Health, Inc.

3. All parent corporations and any publicly held companies that own 10% or more of the stock of any party represented by me are:

None

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

FOLEY HOAG LLP
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5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal:

ChromaDex, Inc. v. Elysium Health, Inc., No. 16-cv-2277 (C.D. Cal.);
ChromaDex, Inc. et al. v. Elysium Health, Inc., No.18-cv-1434 (D. Del.)

Dated: October 9, 2019

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I. INTRODUCTION

After Elysium filed its opening brief, Dartmouth abandoned its cross-appeal from the Board's determination that four of the five claims of the '086 patent are anticipated by the prior art. Dartmouth thus concedes that the inventions claimed in claims 1, 3, 4 and 5 of the '086 patent were described in scientific publications co-authored by Dr. Joseph Goldberger nearly 100 years ago. More particularly, Dartmouth admits, expressed in the language of the claims, that the processed milk products administered by Goldberger in the 1920s constituted pharmaceutical compositions comprising nicotinamide riboside (NR) in admixture with a carrier, and that these milk products increased NAD+ biosynthesis upon oral administration.

The only issue remaining on appeal is whether the NR in Goldberger's milk products meets claim 2's source limitation, "is isolated from a natural or synthetic source." If so, then claim 2, the only remaining claim of the '086 patent, likewise is anticipated by each of the Goldberger references. The NR in Goldberger's milk products indisputably came from a natural source, and it was isolated from that natural source within the meaning of the specification's express definition of an isolated molecule. Claim 2 therefore is anticipated, and the Board's contrary determination must be reversed.

To avoid anticipation, Dartmouth relies on an untenable claim construction, urging that a 25% purity requirement must be grafted onto the phrase "is isolated"

in claim 2. This argument ignores the plain meaning of the specification and violates the most fundamental canons of claim construction, which dictate that the specification's express definitions control and that importation of limitations into the claims is prohibited. Dartmouth's argument also ignores the Board's obligation to construe claim 2 under the "broadest reasonable interpretation."

Dartmouth's attempt to read a 25% purity limitation into claim 2 finds no support in the evidentiary record. Before the Board, Dartmouth, whose patent attorneys drafted claim 2, initially urged the Board to adopt a much broader construction of "is isolated"— a construction that included no purity limitation whatsoever. Dartmouth later abandoned its written understanding of "is isolated" to adopt the added purity requirement espoused in the Board's Institution Decision. Tellingly, when it did so, Dartmouth made no attempt to support the Board's construction through expert testimony or any other form of evidence.

Lacking any evidentiary basis for its argument, Dartmouth instead relies on inapt and conclusory assertions about the '086 patent's specification. It also relies on bald attorney argument purporting to explain the skilled artisan's understanding of the specification, proclaimed with no record citations at all. A 25% purity limitation cannot be read into the claims simply on the say so of Dartmouth's litigators.

Reviewing the Board's claim construction de novo under the broadest reasonable interpretation standard, this Court should hold that Elysium's proposed

construction of claim 2 is reasonable and adopt it. Under that construction, it is undisputed that both prior art Goldberger references anticipate claim 2. Accordingly, this Court should reverse the Board's erroneous construction of claim 2 and rule that the claim is invalid.

II. ARGUMENT

A. The Board's Construction of Claim 2 Must Be Reversed

Under the broadest reasonable interpretation standard, the Board's narrow claim construction must be reversed because Elysium's broader construction is reasonable; nothing in Dartmouth's Responsive Brief demonstrates otherwise. *See, e.g.*, *PPC Broadband, Inc. v. Corning Optical Communs. RF, LLC*, 815 F.3d 734, 742 (Fed. Cir. 2019) (affirming construction that was "not unreasonable"); *see also Google LLC v. Network-1 Tech., Inc*., 726 Fed. Appx. 779, 785 (Fed. Cir. 2018) (explaining that "under the broadest reasonable construction standard, where two claim constructions are reasonable, the broader construction governs"). Elysium's proposed construction tracks the express definition of "an isolated molecule" in the '086 patent and is consistent with the purpose of dependent claim 2, which is to add a source requirement for the NR recited in claim 1. In contrast, Dartmouth's post hoc decision to embrace the Board's 25% purity requirement over its earlier, broader interpretation lacks any basis in the claim language or specification and is not supported even by Dartmouth's own expert testimony.

1. The Specification's Express Definition Controls

Dartmouth's Responsive Brief relies on an illogical and ungrammatical reading of the specification to re-write the express definition of "isolated molecule" to require that ***any*** isolated molecule must be at least 25% pure (w/w).

The specification defines an isolated molecule as follows:

> As used herein, an ***isolated molecule*** (e.g., an isolated nucleic acid such as genomic DNA, RNA or cDNA or an isolated polypeptide) ***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.

(Appx51 (9:3-9:10) (emphasis added).) This definition contains no purity requirement. Instead, it specifies that a molecule is "isolated" for purposes of the patent whenever the molecule is "separated or substantially free from at least some of the other components of the naturally occurring organism." Nothing more is required.

The sentence that follows the definition of "an isolated molecule" adds a purity requirement for a ***subset*** of isolated molecules, namely molecules that are polypeptides:

> ***When 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).

(Appx51 (9:10-9:12) (emphasis added).)

It is undisputed that NR is ***not*** a polypeptide. The Board found as much and Dartmouth does not argue otherwise. (Appx14, Appx1151.) According to the

plain meaning of the specification and basic rules of English grammar, the purity requirement that applies "[w]hen the isolated molecule is a polypeptide" does not also apply when the isolated molecule is ***not*** a polypeptide. If the patent applicant had meant for the purity requirement to apply to all molecules, it would not have used the linguistic formulation that appears in the '086 patent.

Dartmouth's Responsive Brief does not explain how a coherent interpretation of these two sentences of the specification could lead to the conclusion that a 25% purity requirement should apply to ***all*** isolated molecules. Instead, Dartmouth relies on attorney argument that cannot be squared with the language of the specification. For example, Dartmouth writes that the first sentence "includes an explanation of 'isolated molecules' generally" and argues that the second sentence "then explains what it means for a molecule to be 'separated or substantially free' (i.e., 'isolated), ***using a polypeptide as an example***." Dartmouth Responsive Brief at 7-8 (emphasis added). Dartmouth does not attempt to explain its syntactical sleight-of-hand. Nothing in the second sentence remotely suggests that it sets forth a requirement covering all isolated molecules by using polypeptides "as an example."

If the applicant intended the second sentence to apply to all molecules, there would have been no need for "an example." Instead, the applicant would have written: "An isolated molecule is at least about 25%, 50%, 60%, 70%, 75%, 80%, 85%, 90%,

95%, 97%, 98%, 99% or more pure (w/w)." This would have resulted in a narrower claim 2, but Dartmouth elected instead to define isolated molecule broadly, with no minimum purity requirement, giving its claims greater scope and helping to defeat any future third party non-infringement contentions. Having made that choice during prosecution, Dartmouth did not even suggest that a purity requirement should be read into claim 2 when it presented its Preliminary Response to Elysium's IPR Petition. (Appx1150.)

Contrary to Dartmouth's argument, the Board's purity requirement cannot be justified on the theory that it explains what it means for a molecule to be "separated or substantially free." As an initial matter, the express definition of an isolated molecule does not require "additional explanation." The specification states in plain English that an isolated molecule "means a molecule separated or substantially free from ***at least some*** of the other components of the naturally occurring organism . . . ." (Appx51 (9:3-8) (emphasis added).) These words are clear and unambiguous, and there is no evidence, including from Dartmouth's own expert, that a person of ordinary skill in the art would be confused about their meaning or believe that they amounted to a specific purity limitation of at least 25%.

2. The Board's Focus on the Wrong Relationship Underscores the Error in its Claim Construction

The Board's importation of the polypeptide purity requirement into claim 2 does not illuminate the meaning of "separated or substantially free" for other

reasons. As explained in Elysium's opening brief, the Board's purity requirement focuses on the relationship between NR and the rest of the pharmaceutical composition, whereas the language of the definition—"separated or substantially free from" —focuses on the relationship between NR and other molecules naturally associated with NR in the source material. *See* Elysium Opening Brief at 23-24.

Recognizing that this aspect of the Board's construction cannot be justified, Dartmouth does not even attempt to defend it. Instead, Dartmouth challenges Elysium's understanding of the Board's ruling and argues that the Board's construction actually "focuses on the NR in relation to the source from which that NR was obtained." Dartmouth Responsive Brief at 32. Dartmouth's argument concedes that interpretation of "isolated" in claim 2 must focus on the relationship between the NR in the claimed pharmaceutical composition and the other components in the NR source material.

But Dartmouth's assertion that the Board in fact focused on this relationship is a leap too far. The Board construed "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***." (Appx1152 (emphasis added).) The antecedent of "the composition" is the pharmaceutical composition of claim 1. This is clear from the plain language of claim 2, which begins by reciting "The pharmaceutical composition of claim 1 . . ."

It is also shown from the remainder of the Board's Final Written Decision, in which the Board repeatedly uses the word "composition" to refer to the claimed "pharmaceutical composition." (Appx9, Appx10, Appx30, Appx41.) Similarly, when applying its construction to the Goldberger prior art, the Board analyzed whether the ***pharmaceutical compositions***—*i.e.*, the milk products—disclosed in those references contain 25% NR (w/w). The Board stated, for example: "We have found no persuasive evidence in the record to show that NR constituted at least 25% (w/w) ***of the skim milk*** used by Goldberger et al." (Appx26 (emphasis added); *see also* Appx38.) As Elysium explained in its opening brief, under the Board's erroneous analysis, the amount of a filler added to a tablet containing 1 mg NR would determine whether the NR is "isolated" for purposes of claim 2. If the tablet contains 2.9 mg of filler (leaving 25% NR w/w), the NR is isolated, but if it contains 3.1 mg of filler, the NR represents less than 25% w/w of the composition and therefore is not isolated.

Dartmouth's Responsive Brief seems to contend that, under the Board's construction, NR is "isolated" when ***the product of an isolation step*** is 25% NR, whether that product is the pharmaceutical composition or not.[1] Under that

[1] *See, e.g.*, Dartmouth Responsive Brief at 33 (arguing that the "correct relationship" is the "purity level of NR when it is isolated from the source of that molecule").

interpretation, skim milk would not contain "isolated" NR because the product of the isolation step—the remaining skim milk after the fat is removed from whole milk—is not 25% NR. However, if the NR in the skim milk is completely removed to form a pellet that is 100% NR and the pellet is then added back into the skim milk from which it was removed, the skim milk would now contain "isolated" NR under Dartmouth's theory. Thus, according to Dartmouth, two glasses of molecularly-identical skim milk, with exactly the same amount of NR separated from a natural source, would be treated differently under claim 2. Dartmouth's argument is illogical, ungrammatical, and cannot be correct given that the claim is directed to the composition itself, not a method of manufacturing the composition.

Dartmouth's theory effectively converts claim 2 into a product-by-process claim to a pharmaceutical composition made by a process that requires, at some point in the manufacturing process, that the direct product of an isolation step contain at least 25% NR. Under Dartmouth's theory, the direct product of an isolation step does not have to be the claimed pharmaceutical composition and instead can be the result of any intermediate step in the process of making the pharmaceutical composition. There is nothing in the language of claim 2 to justify construing it as a product-by-process claim, and the Board did not so find.

Moreover, and in any case, if claim 2 were construed as a product-by-process claim, it still would be anticipated by the Goldberger references. "It has

long been established that one cannot avoid anticipation by an earlier product disclosure . . . by claiming the product as produced by a particular process." *See SmithKline Beecham Corp. v. Apotex Cop.*, 439 F.3d 1312, 1318 (Fed. Cir. 2006). If one of the glasses of molecularly-identical skim milk discussed above would anticipate a product-by-process claim, then the other glass likewise would anticipate. Because the skim milk whose NR was completely isolated from its source and then added back into the skim milk would anticipate even under Dartmouth's theory, the skim milk administered in the Goldberger reference also anticipates.

3. The Remainder of the Specification Does Not Support Importing a 25% Purity Requirement into Claim 2

As Dartmouth's brief recognizes, the terms "isolated" and "isolating" appear nearly fifty times in the specification of the '086 patent. *See* Dartmouth Responsive Brief at 7. Yet the ***only*** instance in which the terms "isolated" or "isolating" are linked to a 25% purity requirement is the single reference in column 9 to isolated molecules that are ***polypeptides***. Lacking any support for importing a purity requirement into a claim in which the isolated molecule is ***not*** a polypeptide, Dartmouth resorts to sweeping generalizations about "the rest of the specification" or "the remainder of the specification" without citing specific disclosures or explaining how they support Dartmouth's claim construction position. *See* Dartmouth Responsive Brief at 21, 23. Such conclusory assertions, untethered to

any particular disclosure in the specification or the record, are not grounded in evidence and should be ignored.

In all, Dartmouth's Responsive Brief cites only ***one*** other passage of the specification as support for the Board's construction: the NR testing method discussed in columns 26 and 27. As Elysium explained in its opening brief, this method is designed to determine whether a potential natural source of NR (*e.g.*, meat) or potential synthetic source of NR (*e.g.*, a chemical library) does or does not contain NR.[2] The specification explains that "isolated extracts" of potential natural sources can be used in this NR identification test. The specification also lists some exemplary ways in which the isolated extract of the potential natural source can be prepared.

As Elysium explained in its opening brief, the NR testing method cannot be twisted into a 25% purity requirement for claim 2 because the testing method has nothing to do with the subject matter of claim 2 and does not mention a 25% purity requirement or any other purity requirement. *See* Elysium Opening Brief at 20-23. Elysium also explained that there is no factual basis for finding that the exemplary methods for preparing the isolated extracts will produce an extract in which NR

[2] Dartmouth's bald assertion that Elysium "ignored" this passage is false. Dartmouth Responsive Brief at 23. Elysium's opening brief addressed the passage at length. *See* Elysium Opening Brief at 20-23.

constitutes at least 25% of the composition. *See id*. Dartmouth's Responsive Brief offers no evidence or substantive argument to dispute with any of this. Instead, Dartmouth simply quotes the passage discussing preparation of isolated extracts and then uses the phrase "in other words" as a substitute for legal argument.

Beginning with its quote from the specification, Dartmouth states as follows:

> Synthetic sources of nicotinamide riboside can include any library of chemicals commercially available from most large chemical companies including Merck, Glaxo, Bristol Meyers Squibb, Monsanto-Searle, Eli Lilly and Pharmacia. Natural sources which can be [tested] for the presence of a nicotinamide riboside include, but are not limited to, cow's milk, serum, meats, eggs, fruit and cereals. Isolated extracts of the natural sources can be prepared using standard methods. For example, the natural source can be ground or homogenized in a buffered solution, centrifuged to remove cellular debris, and fractionated to remove salts, carbohydrates, polypeptides, nucleic acids, fats and the like before being tested on the mutant[] strains of the invention. Any source of nicotinamide riboside that scores positively in the assay of the invention can be further fractionated and confirmed by standard methods of HPLC and mass spectrometry.
>
> Appx59-60 (26:64-27:12); see also Appx62-63 (32:54-33:2, Example 2 describing "Nicotinamide Riboside and Whey Preparations"); Appx56 (19:5-28, describing purification techniques for NR kinases). ***In other words***, and as the Board recognized, these teachings would convey to a person of ordinary skill in the art "that isolating NR is more than simply separating or rendering it substantially free from any amount of the other components of the naturally occurring organism." Appx14.

Dartmouth Responsive Brief at 23-24 (emphasis added). Dartmouth repeats these conclusory assertions later in its brief, again using the phrase "in other words" to

introduce unfounded assertions about the views of a person of ordinary skill in the art. *See id*. at 30-32. Dartmouth does not articulate ***any*** basis for its characterization of what the NR testing method conveys to a person of ordinary skill in the art. And for good reason: Dartmouth offered no expert testimony about the testing method, there is no other support in the record for Dartmouth's assertion, and the language of the specification contradicts Dartmouth's ipse dixit characterization.

First, the NR testing method discusses the preparation of a test sample, not the manufacture of a pharmaceutical composition comprising NR isolated from a natural source. There is no reason that a person of ordinary skill in the art, in interpreting claim 2, would ignore the specification's express definition of an isolated molecule in favor of a vague discussion eighteen columns later concerning the preparation of food extracts as test samples.

Second, the specification explains that when testing a potential natural source for the presence of NR, the potential source can be prepared using "standard methods" and then provides some exemplary methods, not an exhaustive list. Dartmouth's attempt to read into claim 2 the alleged result of using these non-exclusive testing methods would be improper even if the methods were related to claim 2 (they are not) and reliably yielded samples with 25% NR (they do not). *See, e.g., i4i Ltd. P'ship v. Microsoft Corp*., 598 F.3d 831, 844 (Fed. Cir. 2010) (permissible language in specification does not limit claim scope).

Third, there is no evidence whatsoever that the exemplary methods recited for preparing a sample extract will yield an extract with 25% NR. Dartmouth's assertion that the methods would likely remove "much more than 25%" of the source material is made up out of whole cloth and baldly presented to this Court without any record citation whatsoever. Dartmouth Responsive Brief at 25. Dartmouth offered no expert testimony to this effect, and if the Board had made such a finding it would have been reversible error because there is no *evidence* to support it.

What is more, even if, contrary to all the evidence, a person of ordinary skill in the art were to read a purity requirement into claim 2 based on the disclosed NR testing method, why would she not set that level at 15% or 2% or a fraction of 1%? There is no guidance in the specification that would lead the skilled artisan to conclude that claim 2 requires at least ***25%*** purity—or any other specific level of purity.[3] In fact, the purpose of the method is to determine whether the isolated food extract has any NR at all. Because a food sample might have no NR, the NR in the isolated extract prepared according to the exemplary methods equally could be 0.0%.

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[3] The one document cited by Dartmouth as evidence of the alleged commercial embodiment of "isolated NR," which is sold under the name Niagen®, expressly states that the "maximum use level" of Niagen is ***0.027%*** by weight. Dartmouth Responsive Brief at 3 (citing Appx1597).

More fundamentally, there is no description anywhere in the specification, including in the passage discussing the NR testing method, disclosing that the inventors measured the w/w purity of NR in a pharmaceutical composition after isolating it from a natural or synthetic source. If claim 2 really were directed to a pharmaceutical composition having a particular NR purity, the specification would need to demonstrate possession of such a composition. It does not.

Fourth, Dartmouth submitted no extrinsic evidence showing how a person of ordinary skill in the art would interpret this passage of the specification. Dartmouth did file an expert declaration by Dr. Zhaohui Sunny Zhou in support of its Patent Owner Response. (Appx1316.) His declaration discussed the specification of the '086 patent and offered opinions on the meaning of one claim term. (Appx1324-1328.) However, the declaration did not address either the meaning of "isolated" in claim 2 or the specification's discussion of the NR testing method, let alone opine on what that the exemplary testing methods "would convey to a person of ordinary skill in the art." In the IPR proceedings below, Dartmouth made the strategic decision to forego any attempt to develop evidence in support of the Board's construction of claim 2, and it cannot now substitute attorney argument on appeal for record evidence below.

Fifth, the cited passage is entirely consistent with Elysium's proposed construction because the "isolated extracts" of food samples discussed therein

indisputably are "separated or substantially free from at least some of the other components of the naturally occurring organism." The Board could not have relied on this passage to conclude that Elysium's proposed construction was unreasonable.

4. Elysium's Proposed Construction is Consistent with the Purpose of Claim 2

Dartmouth's Responsive Brief argues that Elysium's proposed construction is "unreasonably broad." Dartmouth Responsive Brief at 25. On the contrary, Elysium's construction is reasonable and consistent with the purpose of dependent claim 2, which is to narrow claim 1 by specifying two potential sources of the NR recited in claim 1.

The specification of the '086 patent states that "a nicotinamide riboside composition" can be used to prevent or treat disease. (Appx60 (28:2-15).) The specification then explains that the NR can be sourced "from a natural or synthetic source" or it "can be chemically synthesized." (Appx60 (28:16-21).) Claim 1 of the '086 does not limit the source of the NR in the claimed pharmaceutical composition. Dependent claim 2 narrows claim 1 by adding a source requirement: the NR in the pharmaceutical composition of claim 1 must be isolated from a natural source or a synthetic source (not chemically synthesized). Seen in this light, Dartmouth's proposed construction is untenable. If the applicant truly intended for claim 2 to add both a source limitation and a purity requirement, it would have said so explicitly in the claim.

Dartmouth's argument that Elysium's proposed construction is unreasonably broad boils down to the assertion that the composition of claim 2 cannot encompass processed milk products because the specification of the '086 patent identifies milk as one of many natural sources of NR. ***But Dartmouth now concedes that the processed milk products administered in the Goldberger references anticipate claims 1, 3, 4, and 5 of the '086 patent.*** This is law of the case. Dartmouth has waived any disagreement that the buttermilk and skim milk in the Goldberger references constitute pharmaceutical compositions comprising NR as claimed in claim 1 of the '086 patent.

Because the NR in buttermilk and skim milk is isolated from a natural source, it is only reasonable to conclude that claim 2, when properly construed, likewise is anticipated by those same references. The applicant's recognition in the '086 patent that milk is a source of NR does not change the undisputed fact that nearly 100 years before the '086 patent was filed, milk was the source of NR in products that were used to prevent and treat pellagra. Dartmouth cannot now argue that claim 2 cannot be construed to encompass compositions of skim milk and buttermilk while at the same time conceding that claims 1, 3, 4, and 5 all are anticipated by compositions of skim milk and buttermilk, as the Board found.

In opposing Elysium's claim construction, Dartmouth repeatedly returns to an issue that is not before this Court on appeal—whether ***unprocessed whole milk***

anticipates claim 2. Neither Goldberger reference discloses the administration of unprocessed whole milk; they both concern the use of processed milk products—skim milk and buttermilk—to prevent and treat pellagra. Because the NR in skim milk and buttermilk is indisputably separated from at least some of the other components of whole milk, Elysium's arguments on appeal properly focus on those processed milk products. Moreover, in using whole milk as the source of NR, the processed milk products described in the Goldberger prior art embody exactly what Dartmouth claims the '086 specification discloses. Dartmouth's argument about whole milk is a red herring that is irrelevant to this appeal.

5. The Board's Fallback Interpretation of Claim 2 is Erroneous

As Elysium explained in its opening brief, the Board's analysis of the patentability of claim 2 first applied its narrow construction of "isolated," requiring 25% w/w purity. It then applied a second, alternative construction that, as Dartmouth concedes, would require that every other component present in a natural source of NR—*i.e.*, all "salts, carbohydrates, polypeptides, nucleic acids, fats and the like" —"must be removed" in the isolation process. *See* Elysium Opening Brief at 24-26. This extreme and even narrower construction, requiring 100% pure NR, was not asserted by either party, just as neither party proposed the Board's first construction. The Board's alternative construction is

equally erroneous, and it flatly contradicts the specification's express definition requiring that the isolated molecule be "separated or substantially free from ***at least some*** of the other components" (*i.e.*, not ***all*** of them). (Appx51 (9:3-8) (emphasis added).)

Dartmouth's Responsive Brief discusses the Board's fallback claim construction in a single paragraph, in which Dartmouth approvingly summarizes the alternative construction without attempting to defend it. *See* Dartmouth Responsive Brief at 36. Dartmouth repeats the Board's reference to language in the specification describing exemplary methods for preparing food extracts to test for NR, but it does not say how that language could justify the Board's fallback construction. For the reasons given above, the cited passage cannot be used to import limitations into the phrase "is isolated" in claim 2's source limitation.

Elysium's opening brief presented further reasons why this passage does not support the Board's fallback construction; Dartmouth's Responsive Brief does not respond to them. For example, Dartmouth does not address the specification's statement that "[a]ny source of nicotinamide riboside that scores positively in the assay of the invention can be ***further*** fractionated and confirmed by standard methods of HPLC and mass spectrometry." (Appx60 (27:9-27:12) (emphasis added)). Dartmouth's Responsive Brief does not dispute that this statement means that samples prepared for testing may contain other components, contrary to the

Board's fallback construction. *See* Elysium Opening Brief at 26. Dartmouth's failure to engage Elysium's criticisms of the Board's analysis underscores that the Board's faulty reasoning cannot be defended.

6. This Court's Precedent Compels Reversal of the Board's Claim Construction

a. Dartmouth's Responsive Brief fails to distinguish *Martek* and *Braintree Laboratories*

In its opening brief, Elysium reviewed this Court's decisions in *Martek* and *Braintree Laboratories* to show that the Federal Circuit reverses claim construction rulings that disregard an express definition in the specification. In *Martek*, this Court reversed a claim construction that altered the express definition of the term "animal" so that it excluded humans. The Court held that the express definition, which contains no such exclusion, must control. *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1380 (Fed. Cir. 2009). Dartmouth incorrectly argues that *Martek* does not apply on the theory that, in this case, "the Board adopted the definition of 'isolated' without changing any of the terms or language expressly recited in that definition." Dartmouth Responsive Brief at 28. Dartmouth's characterization of the Board's decision simply is false: the Board unquestionably altered the definition of "isolated molecule" expressly recited in the specification to add a purity requirement that, according to the language of the specification, applies only to isolated

polypeptides. Dartmouth concedes as much when it says that the Board's construction "only ***adds*** a purity level" to the express definition. *Id*. (emphasis added).

In *Braintree Laboratories*, this Court reversed a claim construction ruling in which the district court replaced the word "or" in a specification's express definition with the word "and." *Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d 1349, 1356 (Fed. Cir. 2014). Dartmouth incorrectly urges that *Braintree* is distinguishable on the theory that the phrase "separated or substantially free" in the express definition of "isolated molecule" requires "additional explanation," and that the phrase must be understood to add a 25% purity requirement for all categories of isolated molecules. Dartmouth Responsive Brief at 29. As explained above, the specification's express definition does not require "additional explanation," and the Board's purity requirement, importing into the claim a requirement that the applicant expressly limited to polypeptides, does not "explain" the express definition. Rather, as Dartmouth concedes, the Board's purity requirement is an "additional feature" not recited in the definition. *Id.*

b. The cases Dartmouth cites do not apply

To support its argument that a purity requirement should be imported into claim 2, Dartmouth cites two cases whose facts are very different from the facts of this case. In *Trading Techs., Int'l, Inc. v. eSpeed*, *Inc.*, this Court considered the

meaning of the term "static." 595 F.3d 1340, 1353 (Fed. Cir. 2010). The specification stated: "The values in the price column are static; that is, they do not normally change positions unless a re-centering command is received (discussed in detail later)." *Id*. Holding that the "re-centering command" must be "manual," the *Trading Technologies* court relied on several aspects of the patent-in-suit that are not present in the '086 patent, including:

- the specification's definition "expressly promises to discuss 'a re-centering command . . . later' in the specification" and "[f]rom that point forward, the specification only discusses manual re-centering commands";
- the specification refers to "the present invention" as involving a manual input; and
- each of the claims of one of the patents-in-suit includes a "wherein" clause expressly excluding software that automatically re-centers.

Id. at 1353-54. In contrast, the '086 patent's express definition does not promise greater detail later in the specification; the '086 patent does not state that "the present invention" is a pharmaceutical composition comprising 25% NR; and nothing in the claims suggests that a 25% purity requirement is appropriate.[4]

[4] The *Trading Technologies* court also affirmed the district court's decision that the price axis "never" changes unless by manual re-centering. *Id*. at 1354-55. A

In *Abraxis Bioscience, Inc. v. Mayne Pharma Inc.*, this Court considered the proper construction of the claim term "edetate." 467 F.3d 1370, 1375 (Fed. Cir. 2006). The specification stated: "By the term 'edetate' we mean ethylenediaminetetraacetic acid (EDTA) and derivatives thereof . . . ." *Id*. at 1376. This Court held that "derivatives" of edetate are EDTA salts or compounds that maintain the EDTA free acid structure and do not encompass structural analogs of edetate. *Id*. at 1377-78. The Court explained that the specification lists EDTA salts as "[p]articular derivatives of use in the present invention," emphasizes the applicants' discovery that EDTA salts were successful in the context of the claimed invention, and describes EDTA salts as "advantageous, preferable, and exceptional." *Id*. at 1377. The Court found that construing "derivatives" broadly to encompass "a large number of non-derivative compounds" would be inconsistent with these statements in the specification and would "fail[] to recognize that the patentees' discovery focused on the unexpected effectiveness of edetate and its salts as antimicrobial agents." *Id*. at 1377-78.

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contrary construction "would defy the invention's goal" and contradict statements made during prosecution to overcome an indefiniteness rejection. *Id*. In contrast, Elysium's proposed construction is consistent with claim 2's goal of narrowing the scope of the pharmaceutical composition of claim 1 of the '086 patent by adding an NR source limitation. Dartmouth does not contend that Elysium's construction would in any way clash with the prosecution history of the '086 patent, and it would not.

In contrast, the '086 patent does not even describe a pharmaceutical composition comprising 25% NR, let alone emphasize the uniquely successful or "advantageous, preferable, and exceptional" qualities of such a composition. Dartmouth's alleged discovery did not focus on the effectiveness of a composition comprising 25% NR, and there is nothing in the specification of the '086 patent that is inconsistent with Elysium's proposed construction of "isolated." In short, the facts of *Abraxis* are entirely different from the facts of this case.

B. Claim 2 is Anticipated Under Elysium's Proposed Claim Construction

As explained in Elysium's opening brief, the evidence establishes that claim 2 is anticipated by each of the two Goldberger prior art references (Goldberger et al.[5] and Goldberger and Tanner[6]) under Elysium's proposed construction of that claim. *See* Elysium Opening Brief at 27-28. Dartmouth did not argue otherwise before the Board, and it has now accepted the Board's determination that the Goldberger references anticipate every other claim of the '086 patent. Elysium's opening brief demonstrated that Elysium's proposed claim construction is reasonable, that the Court should find claim 2 invalid under Elysium's construction, and that, accordingly, a remand is unnecessary. *See id*.

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[5] Appx655-725.

[6] Appx726-747.

Dartmouth's Responsive Brief does not disagree. Dartmouth never attempts to show that claim 2 is valid under Elysium's claim construction, nor does it argue for remand in the event that this Court adopts Elysium's proposed construction. Instead, Dartmouth's "no anticipation" argument is limited to the application of the Board's claim construction and the Board's fallback construction.[7] If this Court adopts Elysium's construction, it should find that claim 2 is anticipated by each of Goldberger et al. and Goldberger and Tanner.

This Court should reject Dartmouth's last-ditch effort to avoid invalidity by urging the Court to find claim 2 not anticipated by the Goldberger references under "whatever definition is used for 'isolated.'" Dartmouth Responsive Brief at 38. This argument simply reprises Dartmouth's erroneous and misleading argument, discussed above, that "isolated" cannot be construed to encompass processed milk products. Contrary to Dartmouth's claim, the specification makes clear that NR is

[7] In its Summary of Argument, Dartmouth states: "Under either construction"—presumably referring the constructions of the Board and Elysium—"the prior art references do not contain any disclosure of NR, let alone any disclosure of the purity of the NR with respect to the source of the molecule." Dartmouth Responsive Brief at 18. Dartmouth waived any argument that the Goldberger references do not disclose compositions comprising NR when it dropped its appeal of the Board's determination that they do, which may be why Dartmouth does not attempt to articulate this argument in the Argument section of its brief. Dartmouth's reference to a "disclosure of the purity of NR" is not relevant to anticipation under Elysium's proposed construction.

"isolated" when it is separated or substantially free from at least some of the other components of the naturally occurring organism. As Elysium's expert explained—without challenge from Dartmouth—this is what happens to NR when skim milk and buttermilk are made.

Dartmouth says that "the specification makes clear that one cannot achieve isolated NR simply by skimming fat off of milk." Dartmouth Responsive Brief at 37. But it cites no evidence to support this conclusory attorney argument. If Elysium's position were so baseless, surely Dartmouth's expert would have said so in his sworn declaration. This Court should not accept Dartmouth's invitation to adopt a results-oriented, hindsight approach, which begins with Dartmouth's position that claim 2 should be considered novel over the prior art and then works backward to find a claim construction that will lead to Dartmouth's preferred outcome.

Finally, Dartmouth's argument that milk cannot anticipate claim 2 because the specification purportedly "disavows the scope that cow's milk could include isolated NR" and distinguishes milk from "the present invention" simply repackages Dartmouth's erroneous claim construction arguments as baseless arguments against invalidity. Dartmouth Responsive Brief at 38-39. The specification makes no mention of skim milk, buttermilk, or any other derivative of whole milk, so it could not "disavow" or "distinguish" claim scope as to them.

Dartmouth's arguments based on one particular reference to the "present invention" are misguided because the specification uses the phrase "present invention" ***41 times***, but not once refers to a pharmaceutical composition comprising 25% NR (w/w) as a "present invention." Moreover, as discussed at length above, the NR testing methods do not "distinguish[] the 'isolated NR' of claim 2 from cow's milk." Dartmouth has conceded that the milk products disclosed in the Goldberger references anticipate claims 1, 3, 4, and 5. This Court should hold that claim 2 is anticipated as well.

III. CONCLUSION AND RELIEF SOUGHT

For all the foregoing reasons, this Court should reverse the Board's construction of claim 2, adopt Elysium's proposed construction of that claim, and hold that claim 2 is anticipated both by Goldberger at al. and by Goldberger and Tanner. In the alternative, the Court should remand the case to the Board to reconsider Elysium's challenge to the validity of claim 2 under the correct construction of that claim.

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CERTIFICATE OF SERVICE

I hereby certify that on October 9, 2019, the foregoing Reply Brief of Appellant was electronically filed through this Court's CM/ECF system, which will send a notice of filing to all registered users.

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