No. 2018-1295

In the United States Court of Appeals for the Federal Circuit

NATURAL ALTERNATIVES INTERNATIONAL, INC.,

Plaintiff-Appellant,

v.

CREATIVE COMPOUNDS, LLC,

Defendant-Appellee,

DOES 1-100; CORE SUPPLEMENT TECHNOLOGIES, INC.; HONEY BADGER, LLC; MYOPHARMA, INC.,

Defendants.

Appeal from the United States District Court
for the Southern District of California, Case No. 3:16-cv-02146-H-AGS.
The Honorable **Marilyn L. Huff**, Judge Presiding.

BRIEF OF *AMICUS CURIAE* PATENT LAW SCHOLARS IN SUPPORT OF PLAINTIFF-APPELLANT AND REVERSAL

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Rev. 10/17

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

Natural Alternatives Int'l, Inc. **v.** Creative Compounds, LLC

Case No. 2018-1295

CERTIFICATE OF INTEREST

Counsel for the:
☐ (petitioner) ☐ (appellant) ☐ (respondent) ☐ (appellee) ■ (amicus) ☐ (name of party)

Patent Law Scholars

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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. *See* Fed. Cir. R. 47. 4(a)(5) and 47.5(b). (The parties should attach continuation pages as necessary).

None

4/20/2018
Date

/Kevin E. Noonan/
Signature of counsel

Please Note: All questions must be answered

Kevin E. Noonan
Printed name of counsel

cc: _____

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INTEREST OF AMICI CURIAE[1]

The *amici curiae* are patent law scholars who teach and write on patent law and policy. As such, they are concerned that the law properly promotes and secures protection for inventions in all technologies, including biotechnology. They have no stake in the parties or in the outcome of the case. The names and affiliations of the members of the *amici* are set forth in Appendix A below.

SUMMARY OF ARGUMENT

The district court's decision in *Natural Alternatives International, Inc. v. Creative Compounds, LLC*, No. 16-cv-02146-H-AGS, (S.D. Cal. Sept. 5, 2017) and *Natural Alternatives International, Inc. v. Hi-Tech Pharmaceuticals, Inc.* No. 16-cv-02343-H-AGS, (S.D. Cal. Sept. 5, 2017), represent an improper application of 35 U.S.C. § 101. The parties in their briefs address the relevant innovation covered by Natural Alternatives' patents,[2] as well as the application of the Supreme Court's and

[1] No party's counsel authored this brief in whole or part; no party or party's counsel contributed money intended to fund preparing or submitting this brief; and no person other than *amici*, their members, or counsel contributed money intended to fund preparing or submitting this brief. Consent was sought from each party. Appellee Creative Compounds expressly withheld its consent to the filing of this brief. Fed. R. App. P. 29(c)(5).

[2] There are six patents at issue in this case. U.S. Patent Nos. 5,965,596 (the '596 patent), 7,504,376 (the '376 patent), 7,825,084 (the '084 patent), 8,470,865 (the '865 patent), and 8,993,610 (the '610 patent) and RE45,947 (the '947 patent). Although the '084 patent is illustrative for most purposes, all six patents are discussed below.

the Court of Appeals for the Federal Circuit's § 101 jurisprudence. Here, *amici* offer additional insight concerning the legal and policy problems with the trial court's decision. Specifically, *amici* contend that Natural Alternatives' claims represent precisely how the patent system should reward discovery of a therapeutic use of a natural compound, and thus their invention should be eligible for patent protection. The Supreme Court has repeatedly emphasized that patents claiming new uses of known drugs or new applications of laws of nature are patent eligible, and these teachings properly applied provide patent eligibility for the kinds of claims at issue in this case. *Assoc. for Molec. Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 594 (2013); *Mayo Collaborative Servs v. Prometheus Labs., Inc.*, 566 U.S. 66, 87 (2012). The district court's decision to the contrary conflicts with the Patent Act as an integrated statutory framework for promoting and securing innovation in the life sciences, as construed by this court as well as by the Supreme Court.

The Supreme Court has recognized that the plain meaning of the language of § 101 indicates that the scope of patentable subject matter is broad. *See Diamond v. Chakrabarty*, 447 U.S. 303, 315 (1980); *Myriad* at 577. This is why the Supreme Court consistently has held that "[t]he § 101 patent-eligibility inquiry is only a threshold test." *Bilski v. Kappos*, 561 U.S. 593, 602 (2010). Accordingly, the "threshold test" of § 101 is necessarily followed by the more exacting statutory requirements of assessing a claim as a whole according to the standard of a person

having skill in the art as to whether it is novel, nonobvious, and fully disclosed as required by the *quid pro quo* offered to inventors by the patent system. *Id.*

Unfortunately, courts have applied the two-step "*Mayo/Alice* test" from the Supreme Court's recent § 101 cases in an unbalanced and legally improper manner. *See Alice Corp. Pty. v. CLS Bank Int'l*, 134 S. Ct. 2347 (2014); *Mayo*, 566 U.S. at 66. These practices of the inferior courts include dissecting claims into particular elements and then construing these elements in highly generalized terms with no evidentiary support. Thus, as happened in this case, a district court all too often merely asserts a conclusory finding that the claim—actually, specific elements dissected out of the claim as a whole—covers ineligible laws of nature or natural products to conclude that a patented invention is ineligible.

The lower courts' unduly stringent and restrictive patent eligibility test under the *Mayo/Alice* test produces results such as the district court's decision in this case. This improper application of the *Mayo/Alice* test inevitably leads to § 101 rejections of patentable product and method inventions; here, the district court rejected an innovative invention in the biotechnology sector that the patent system is most certainly designed to promote. When a patent describes a discovery made by the inventor, even if that invention relates to a natural product or natural law, it should be possible to describe a particular application of that law or discovery that is patent eligible so as to reward the inventor for their efforts.

Furthermore, the improper treatment of the § 101 inquiry as primarily a question of law requiring no evidentiary findings whatsoever, especially when the parties expressly disagree as to what a person having skill in the art would consider routine or ordinary, allows courts to gloss over both what the claims are directed to and what importance limitations beyond the ineligible material may have. *See Berkheimer v. HP Inc.*, 881 F.3d 1360, 1368-69 (Fed. Cir. 2018). This improper characterization of § 101 has sowed indeterminacy in patent eligibility doctrine, and has left inventors and companies in the innovation industries with little predictability concerning when or how courts will dissect claims and make conclusory assertions that they are patent ineligible under § 101.

The court in this case has an opportunity to more properly instruct the lower courts in the manner in which the § 101 analysis should be made, particularly with regard to the role of factual evidence in determining when a claimed application of a natural law or product is routine, well-understood, or conventional and when it is not and thus that the claimed invention is eligible for patenting.

ARGUMENT

I. The Supreme Court has affirmed that the scope of the exceptions to patent eligibility is narrow.

District courts have been improperly applying the *Mayo/Alice* test. Such improper analyses have resulted in a *de facto* patent eligibility doctrine under § 101 that is overly restrictive, particularly for product and process inventions in the life sciences and bio-pharmaceutical fields. Too many inventions are considered by courts to fall under the exceptions to patent eligibility, including when the invention is claimed in precisely the manner necessitated by bio-pharmaceutical innovation. Thus, this court should return to the plain language of § 101 and the Supreme Court's interpretation of the statutory mandate.

Section 101 provides that a patent can be obtained by "[w]hoever invents or discovers any new and useful process, machine manufacture or composition of matter or any new and useful improvement thereof." The expansiveness of these terms suggests that the subject matter covered by the patent laws should be given wide scope. Although laws of nature, physical phenomena, and abstract ideas are judicially defined exceptions to the statutory rule and thus not patentable, the scope of these exceptions is narrow. *See, e.g., Alice*, 134 S. Ct. at 2354 ("[W]e tread carefully in construing this exclusionary principle [of finding claims patent-ineligible under § 101] lest it swallow all of patent law.").

The Supreme Court has repeatedly cautioned against an overly restrictive interpretation of the patent laws, which are enacted by Congress according to the constitutional purpose of promoting progress of the useful arts. Courts "should not read into the patent laws limitations and conditions which the legislature has not expressed." *Diamond v. Chakrabarty*, 447 U.S. at 308 (*citing United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199 (1933)). This is particularly true for § 101. The Supreme Court has repeatedly noted the harms that will flow from unduly restricting subject matter eligibility according to the exceptions. *See, e.g., Alice*, 134 S. Ct. at 2354; *Chakrabarty*, 447 U.S. at 316; *Bilski*, 561 U.S. at 601.

Patent claims using natural products to affect the human body present a particularly salient concern with respect to determining patentable subject matter. Because inventions in this field rely on laws of nature and natural phenomena such claims are easy to analytically dissect and overgeneralize into individual foundational laws of nature or natural phenomenon in addition to the natural product used. These limitations then can be restated at such a high level of generalization to cover even non-natural uses of the product or law of nature. That is not because such inventions are limited to recitations of laws of nature or natural phenomena themselves (which the Supreme Court has properly cautioned against; *see Mayo*, 566 U.S. at 77-78), but because these claims (to uses of natural products to affect the

human body) seek to take advantage of how the natural product will affect the human body when administered in a particular way.

The Supreme Court specifically admonished lower courts and the United States Patent and Trademark Office ("PTO") against an overly restrictive application of § 101 in determining patent-eligibility for claimed inventions. *See Mayo*, 566 U.S. at 71. In its 2012 decision addressing the patentability of a diagnostic method in *Mayo Collaborative Services v. Prometheus Laboratories,* the Supreme Court warned "that too broad an interpretation of this exclusionary principle could eviscerate patent law. For all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas." *Id*. Such limiting principles form a common refrain throughout the Supreme Court's § 101 jurisprudence. *See, e.g., Alice*, 134 S. Ct. at 2354-55 (stating that "an invention is not rendered ineligible for patent simply because it involves an abstract concept" in some of its distinct claim elements); *Mayo*, 566 U.S. at 71-72 (recognizing same); *Diamond v. Diehr*, 450 U.S. 175, 187 (1981) ("[A]n application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection."). The Federal Circuit may need to better articulate this basic premise in applying the *Mayo/Alice* test in assessing the patent eligibility of inventions.

Neither Congress nor the Supreme Court intended to dissuade research in the field of natural products for uses beneficial to mankind. There are millions of natural products and processes that incorporate natural phenomena existing in nature for billions of years, but innovative scientific and therapeutic applications continue to evolve, and should be rewarded with patent protection. Patent-ineligible interpretations of the underlying subject matter will limit the commercial value of these products and will force biotechnology and pharmaceutical firms to restrict or eliminate innovation in these fields (or worse, take steps to minimize disclosure of such inventions).

II. The exceptions to § 101 are narrow because they involve questions of fact uniquely applied to every invention.

The exceptions to subject-matter eligibility are narrow, ensuring the doctrine is limited to its narrow purpose. *See Bilski*, 561 U.S. at 602. And the narrowness of the doctrine is intimately tied up in the fact-specific nature of the inquiry, because it is *how* the law of nature or natural product is applied that renders a particular invention patent eligible. *See id.* at 614.

How the test is to be applied was explicitly recognized in *Diamond v. Diehr*, 450 U.S. at 188 ("Arrhenius' equation is not patentable in isolation, but when a process for curing rubber is devised which incorporates in it a more efficient solution of the equation, that process is at the very least not barred at the threshold by § 101."). The question posed in *Diehr* was how the Arrhenius equation was

incorporated into a claimed invention comprising a new rubber-curing process. *Id*. Once it was established that the patent claim as a whole covered a new method of curing rubber, the Supreme Court properly recognized that the § 101 inquiry was at an end. *Id*. Given the structure and function of the Patent Act, this is the sensible interpretation of the patentability provisions as an integrated statutory framework.

Determining the nature of a product or method, what the invention is, and what is routine or ordinary in the art are all factual questions. *Berkheimer*, 881 F.3d at 1368. Such factual questions were well-presented in *Diehr*, which was on appeal from a denial of the patent application at the PTO. 450 U.S. at 185.

This case, which was decided on a motion to dismiss an infringement action, included underlying factual questions that either remained unanswered and which can be resolved only at a later stage in the litigation, or which the court "assumed away" by over-generalizing the natural law at issue. To properly apply § 101, courts must avoid invalidating patents without reviewing relevant evidence and instead provide well-reasoned opinions that reach the appropriate legal conclusion on the basis of this evidence. For a court to treat a § 101 determination as a pure question of law that can be resolved on a motion to dismiss does violence to the integrated statutory framework of the Patent Act by treating § 101 as the sole legal criterion of patentability.

III. Claims challenged under § 101 must be analyzed "as a whole" to ensure the individual claim terms are not construed in isolation as the invention.

The district court ignored the mandate from the *Alice* Court that "we consider the elements of each claim both individually and 'as an ordered combination.'" *Alice*, 134 S. Ct. at 2355 (quoting *Mayo*, 566 U.S. at 79). This proposition—that courts should assess claim elements individually and as a whole—has been improperly construed by lower courts in the disjunctive, *i.e.*, as equally acceptable alternative approaches in construing claims under § 101. The *Alice* Court, however, used the conjunctive "and," and not an "or"; thus, both methods of claim construction are required by the *Mayo/Alice* test. In considering Appellant's claims as "an ordered combination," *id.*, the claimed methods for diagnosing atherosclerotic cardiovascular disease raise several underlying factual questions.

The claimed products and methods require giving a person an abnormally high amount of the natural product (beta-alanine) to produce a non-natural result (improved muscle performance), which immediately suggests factual questions regarding the limits of how the body uses the natural product and what are the limits of the natural result. The district court in this case repeated the same error of many other courts when it ignored particular claim terms and declared that each of these terms fall within the natural law exception. *See, e.g.*, *Nat. Alts. Int'l, Inc. v. Creative Compounds, LLC,* No. 16-CV-02146-H-AGS, 2017 WL 3877808, at *6 (S.D. Cal.

Sept. 5, 2017) (examining the '084 unit dosage patent). The court recognized that the "inventive concept described in claim 1 of the '084 patent is placing a *specific dosage* of beta-alanine into a human dietary supplement," but then proceeded to only analyze the technical components of putting a dosage together. *Id*. (emphasis added). The district court abdicated its responsibility to follow the proper *Mayo/Alice* test, to inquire further about the prior use of beta-alanine, and to identify factual questions and apply the appropriate presumptions based on the Federal Rules of Civil Procedure. *Id.* at *7; Fed. R. Civ. P. 12(b)(6) and 12(c).

These products and methods, which are best characterized as methods of treatment, contain a combination of claim elements that were not practiced at the time of the invention, making them neither routine, conventional, nor well-understood. Regardless of whether factual arguments regarding the prior use of beta-alanine could ultimately be proved at trial, summarily rejecting them at the motion-to-dismiss stage is categorically inappropriate. Moreover, new uses of natural products will always be governed by scientific and physical laws (and in this case, include the natural product used), which makes the factual analysis of the "something more" in step 2 of the *Mayo/Alice* test imperative to the § 101 inquiry in this case. *See Alice*, 134 S. Ct. at 2354-55. Again, resolution of these factual questions at the pleading stage is inappropriate.

When the district court analyzed each claim limitation individually, it essentially embarked on a fact-based analysis—but it did so without considering any factual evidence. *See Nat. Alts.*, 2017 WL 3877808 at *6-7. In considering without evidence the separate claim limitations, the court could not but ultimately rely on its gut reaction or basic sense of the "gist" of the invention. This violates a fundamental requirement in the Patent Act that has long served to ensure that innovation is properly secure under the law: the patentability tests are to be assessed according to the person having skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005). To allow the § 101 analysis to be conducted devoid of the necessary expert input on relevant factual matters, claim construction, factual conclusions, and proper presumptions based on the Federal Rules of Civil Procedure causes the exceptions to swallow the rule under § 101.

IV. Claiming a pharmaceutical innovation based on a natural product or law in a typical manner will typically be patent eligible.

The Supreme Court has repeatedly warned that the exceptions to patent eligibility should not be allowed to swallow the whole. *See, e.g.*, *Mayo*, 566 U.S. at 71 ("too broad an interpretation of this exclusionary principle could eviscerate patent law"). In the bio-pharmaceutical arts, the Court has particularly cautioned against this problem, noting that new uses of drugs, whether claimed as the product or a method of using the product, are patent eligible so long as the claims reach a particular application. *See id.* at 87 ("Unlike, say, a typical patent on a new drug or

a new way of using an existing drug, the patent claims [in Mayo] do not confine their reach to particular applications of those laws."). Natural Alternatives' claims are directed to precisely the kinds of applications that the patent laws contemplate as patent-eligible biopharmaceutical inventions.

Both the Supreme Court and this court have provided substantial guidance on how pharmaceutical patents can be appropriately limited to be found patent eligible. At step 1 of the *Mayo/Alice* test, the key is determining what the claim as a whole is directed to, recalling the Supreme Court's caution that "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas." *Id.* at 71. Step 2 necessarily focuses on the application of a law of nature, where the Supreme Court has noted that a "typical patent on a new drug or new way of using an existing drug [will] confine [its] reach to particular applications of those laws." *Id.* at 87.

The *Mayo/Alice* framework can be applied in the pharmaceutical context by considering what steps are necessary to turn a natural product or law of nature that may be therapeutically beneficial into a commercially valuable product. At a minimum, an inventor must find a useful way to deliver the natural product to the body or to use the law of nature. Rarely, if ever, will there be a product or law so simple and fundamental, that merely saying "apply it" will be sufficient. *See id.* at 72 ("[T]o transform an unpatentable law of nature into a patent-eligible application

of such a law, one must do more than simply state the law of nature while adding the words 'apply it.'"). For example, if the discovery is a natural product with a therapeutic effect, creating an active dosage form containing a defined amount of the product applies the discovery beyond simply saying "give the drug." Similarly, if the discovery is a natural law or phenomenon, providing specific treatment steps for a particular application of the law is not simply saying "apply it"; rather, it is a new method of treatment. Thus, at step 1, patent claims that are appropriately drafted to the inventor's contribution should necessarily be directed to whatever mode of actually applying the natural product or law that is found in the claims, rather than to the natural law itself.[3]

This Court recently acknowledged precisely this distinction: that a properly drafted claim to a new use of a drug will be directed to a method of treatment, not a natural law. *See Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.* 16-2707 at 28 (Apr. 13, 2018). Specifically, substantively limiting the claim[4] to a method of

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[3] It is important to note that proper drafting is about including the substantive aspects of the invention in the claim, such as the proper form for administering a natural product or the sufficiently detailed application of a law of nature. It is not about relying on the draftsman's art to evade the limits imposed by § 101. *See Parker v. Flook*, 437 U.S. 584, 593 (1978).

[4] Claim 1 of the patent at issue in *Vanda* reads:

> A method for treating a patient with iloperidone, wherein the patient is suffering from schizophrenia, the method comprising the steps of:
>
> determining whether the patient is a CYP2D6 poor metabolizer by:
>
> obtaining or having obtained a biological sample from the patient;

treatment, by including a treatment step dependent upon the law of nature, made a claim patent eligible at Step 1. *Id.* at 28-29. For the claim in *Vanda*, the claim is directed to the application recited in the two "if" limitations, indicating what someone should do with the natural law. Having discovered the natural law, the inventors were in the best position to innovate based on it, by designing a new therapeutic regimen, properly claimed. This key fact was used to distinguish *Mayo*, which claimed merely that the law of nature "indicated" something about the patient; no further treatment steps were claimed. *Id.* at 29-30.

For similar reasons, at step 2 of the *Mayo/Alice* test, properly drafted claims to a new use of a natural product or law will represent an inventive application—"something more"— than a claim to the natural law itself. *See Alice*, 134 S. Ct. at

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> and
> performing or having performed a genotyping assay on the biological sample to determine if the patient has a CYP2D6 poor metabolizer genotype; and
> if the patient has a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount of 12 mg/day or less, and
> if the patient does not have a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount that is greater than 12 mg/day, up to 24 mg/day,
> wherein a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype is lower following the internal administration of 12 mg/day or less than it would be if the iloperidone were administered in an amount of greater than 12 mg/day, up to 24 mg/day.

Vanda at 3-4.

2354. In both *Mayo* and *Myriad*, the Supreme Court explicitly noted the *lack* of new application of a natural product or law. *Myriad*, 569 U.S. at 594, *Mayo*, 566 U.S. at 87. *Vanda* also recognized similar reasoning at both steps 1 and 2 of the *Mayo/Alice* test, confining its step 2 reason to noting that the claims "recite more than the natural relationship between CYP2D6 metabolizer genotype and the risk of QTc prolongation. Instead, they recite a method of treating patients based on this relationship…" *Vanda* at 32.

The patents at issue in this case can be separated into two categories: product claims and method of treatment claims. Although the analysis is similar for both, it will be more enlightening to consider the two categories of claims separately. In general, each patent is limited to only the narrow applications that are the new and inventive use of the natural product.

A. Patents claiming the product all recite typical limitations beyond the product of nature.

Three of the patents[5] at issue are directed to different, specific ways of putting the natural product to a beneficial use. Each of them is directed to turning a natural product into a commercial product with particular properties beyond the natural product *per se*. In other words, the claims contain limitations that are typical for turning a discovery of a natural product or law into a patent eligible bio-

[5] The '376, '084, and '947 patents.

pharmaceutical invention.

Claim 1 of the '084 patent[6] and claim 34 of the '947 patent[7] each show one way of claiming a patentable item that uses a product of nature, by reciting an amount of the natural product to be used. Both claims recite a dosage range (0.4g to 16g per day) that is described in the patent as being particularly effective for its therapeutic purpose. Furthermore, as the district court noted, these dosages are designed to produce unnatural effects in the human body. *Nat. Alts.* at *7. Because the benefit of the product is tied to dosages that produce the desired effects, the claims are directed to the specific dosages, rather than the natural compound itself.

Claim 34 of the '947 patent incorporates another aspect of the commercial product that extends beyond the natural product. It requires the product have a particular purity, by eliminating from the product other chemicals that are involved in the same biochemical pathways. Similarly, claim 6 of the '376 patent[8] specifies

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[6] "A human dietary supplement, comprising a beta-alanine in a unit dosage of between about 0.4 grams to 16 grams, wherein the supplement provides a unit dosage of beta-alanine." *Nat. Alts.* at *6.

[7] "A human dietary supplement for increasing human muscle tissue strength comprising a mixture of creatine, a carbohydrate and free amino acid betaalanine that is not part of a dipeptide, polypeptide or an oligopeptide, wherein the human dietary supplement does not contain a free amino acid L-histidine, wherein the free amino acid beta-alanine is in an amount that is from 0.4 g to 16.0 g per daily dose, wherein the amount increases the muscle tissue strength in the human, and wherein the human dietary supplement is formulated for one or more doses per day for at least 14 days." *Nat. Alts.* at *8.

[8] Claim 6 depends from claims 5 and 1, rewritten here in independent form. "A composition, comprising:

what form the product must take; it must be a sports drink as a supplement for humans (as opposed to a pill or other form).[9]

It order to see why these claims should generally be patent eligible, it will be helpful to trace the reasoning in reverse. Rather than starting from a known claim and assessing its patent eligibility, start from the invented product, and ask what should a claim look like that rewards an inventor who is "in an excellent position to claim applications of the [new] knowledge"? *Myriad* 569 U.S. at 595. Natural Alternatives discovered that overloading the body with purified beta-alanine produced desirable effects in muscle tissue. In order to take advantage of this discovery, the claims should recite specific aspects of the commercial product that are applications of the discovery. There are no other options. Thus, they can claim definable aspects of the product such as dose, form of delivery, or purification levels.

These aspects are precisely what the product patents recite: dosages, purities and forms of delivery. If claiming these aspects cannot confer patent eligibility when

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glycine; and
a) an amino acid selected from the group consisting of a beta-alanine, an ester of a beta-alanine, and an amide of a beta-alanine, or
b) a di-peptide selected from the group consisting of a beta-alanine dipeptide and a beta-alanylhistidine di-peptide.
wherein the dietary supplement or sports drink is a supplement for humans." *Nat. Alts.* at *9.

[9] The court also addresses a method of manufacturing patent, U.S. Patent No. 8,993,610, where the product is defined by its form and purity. *See Nat. Alts.* at *12.

a natural product is included in the claim, then no invention based on a natural product will ever be patent eligible. At step 1 of the *Mayo/Alice* test, claiming a commercial embodiment with these aspects should make the claim directed to the recited aspect (*e.g.*, the dose) or to the commercial product itself. To the extent that a fact finder moves to step 2, the role of limitations such as dose depends on what was known to the skilled artisan,[10] and is thus a factual inquiry not suited for judgment on the pleadings.

B. Patents claiming methods all necessarily recite the non-natural application of the inventors' discovery of a purported law of nature.

In addition to the patents directed to products, there are two patents[11] that claim methods of affecting the human body (commonly referred to as methods of treatment). Each of them is directed to applying a natural law in an unnatural way. Thus, similar to the product patents, the method patents claim the invention in precisely the way an inventor should claim a particular application of their discovery.

[10] For example, what is an overloading dose of beta-alanine?
[11] The '596 and '865 patents.

Claim 1 of the '596 patent[12] and claim 1 of the '885 patent[13] claim methods that derive from the discoveries and inventions discussed above for the product claims: that oversupply of beta-alanine produces desirable results in muscles. By defining the law of nature at too high a level of generality (that beta-alanine produces the claimed effects), the district court brought the non-natural results within the purported law of nature. *See, e.g.*, *Nat. Alts.* at *10 ("ingesting certain levels of beta-alanine, a natural substance, will increase carnosine concentration in human tissue and, thereby, aid in regulating the hydronium ion concentration in the tissue"). This reasoning renders all patents applying these discoveries about the human body

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[12] "A method of regulating hydronium ion concentrations in a human tissue comprising: providing an amount of beta-alanine to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in the human tissue; and exposing the tissue to the blood or blood plasma, whereby the concentration of beta-alanylhistidine is increased in the human tissue." *Nat. Alts.* at *10.

[13] A method of increasing anaerobic working capacity in a human subject, the method comprising:
a) providing to the human subject an amount of an amino acid to blood or blood plasma effective to increase beta-alanylhistidine dipeptide synthesis in the tissue, wherein said amino acid is at least one of:
i) beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide;
ii) an ester of beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide; or
iii) an amide of beta-alanine that is not part of a dipeptide, polypeptide or oligopeptide; and
b) exposing the tissue to the blood or blood plasma, whereby the concentration of beta-alanylhistidine is increased in the tissue,
wherein the amino acid is provided through a dietary supplement.
Nat. Alts. at *10-11.

ineligible.

Again, it is helpful to see the categorical error by analyzing these claims in reverse, starting from the discovery and asking what kind of claim should be available. The inventors discovered that oversupply of beta-alanine produces desirable effects. These effects are not natural because they are caused by non-natural stimuli, the oversupply of beta-alanine.[14] The simplest way to claim that application is to claim a method to produce the effect, reciting the steps that are necessary to produce that effect. Claim 1 of the '596 patent does precisely that, reciting that the method is to increase beta-alanylhistidine levels, and that the necessary step is the effective supply of beta-alanine. The '885 patent goes further, providing additional limitations on the nature of the beta-alanine product to be provided, and thus, could also be found patent eligible based on the product supplied. In both cases, if the inventors could not claim these particular applications, directed to the non-natural effects of beta-alanine oversupply, then there would be no path for any patent to be obtained for any application of these discoveries.

Unfortunately, reasoning like the district court's in this case is all too common. It is easy to over-generalize a claim or ignore factual questions to find that a natural product or law of nature renders a patent claim ineligible. However,

[14] Again, to the extent that what level of beta-alanine is normally supplied, or for any other factual question regarding what constitutes the baseline natural law, these are issues of fact that should not be decided on a motion to dismiss.

realizing that the claims are the best way to claim the discovery at issue, even for typical discoveries, shows that harm can be avoided to the patent system by recognizing that these claims are patent eligible.

V. The failure to consider claims as a whole has resulted in legal uncertainty that undermines the innovation industries relying on stable and effective patent rights.

The improper application of § 101 harms innovators, and is now recognized as a factor in the United States dropping from its position as a global leader in patent protection. The misapplication of the *Mayo/Alice* test, especially when disintegrating claims into their separate elements with resulting conclusory assertions of invalidity, is evidenced by inordinately high invalidation rates. As of June 1, 2017, the invalidation rate under the *Mayo/Alice* test in the lower courts is 61.7%. *See #Alicestorm: April Update and the Impact of TC Heartland on Patent Eligibility*, Bilski Blog (June 1, 2017), *http://www.bilskiblog.com/blog/2017/06/alicestorm-april-update-and-the-impact-of-tc-heartland.html.* This follows naturally from judges and patent examiners only assessing individual claim elements, ignoring other elements that comprise the claim as a whole, and ignoring key factual questions that must be properly considered.

Shortly after *Alice* was decided in 2014, anecdotal reports indicated increased rejections of many patent applications covering innovative therapeutic treatments and diagnostic tests under the *Mayo/Alice* test. *See* Bernard Chao & Lane Womack,

USPTO is Rejecting Potentially Life-Saving Inventions, Law360 (Dec. 18, 2014, 11:05 AM), *http://www.law360.com/articles/604808/uspto-is-rejecting-potentially-life-saving-inventions*. Empirical data now confirms these concerns. For example, one examination unit at the PTO that reviews personalized medicine inventions (Art Unit 1634) rejects 86.4% of applications under the *Mayo/Alice* test. *See* Bernard Chao & Amy Mapes, *An Early Look at Mayo's Impact on Personalized Medicine*, 2016 Patently-O Patent L. J. 10, 12, *http://patentlyo.com/media/2016/04/Chao.2016.PersonalizedMedicine.pdf*.

Additionally, the U.S. Chamber of Commerce recently released its well-known International IP Index for 2018. *See* U.S. Chamber International IP Index, 6th Ed., February 2018, *http://www.theglobalipcenter.com/wp-content/uploads/2018/02/GIPC_IP_Index_2018.pdf* ("2018 Index"). The 2018 Index explicitly states that "the patentability of basic biotech inventions was compromised by the Supreme Court decisions in the 2013 *Molecular Pathology v. Myriad Genetics* and 2012 *Prometheus Laboratories, Inc. v. Mayo Collaborative Services* cases." *Id*. at 8. Given the manner in which courts have been misapplying the *Mayo/Alice* test, as detailed above, the 2018 Index confirms that "[t]here is considerable uncertainty for innovators and the legal community, as well as an overly cautious and restrictive approach to determining eligibility for patentable

subject matter in areas such as biotech, business method, and computer implemented inventions." *Id.*

The 2018 Index further concludes that the current state of § 101 jurisprudence in the U.S. "seriously undermines the longstanding world-class innovation environment in the U.S. and threatens the nation's global competitiveness." *Id.* For many years, the United States was number one in the Index, but it fell to 10th place last year and fell to 12th place this year in the 2018 Index of how global patent systems provide stable and effective security for all innovators. *Id.* at 35-37; *see also* Tiffany Hu, *US Drops to 12th in Patent Protection, Report Says*, Law360 (February 8, 2018, 5:36 PM), *https://www.law360.com/ip/articles/1010617/us-drops-to-12th-in-patent-protection-report-says?nl_pk=a9dc0a3c-f8e7-433d-94fe-ac6c396d5149&utm_source=newsletter&utm_medium=email&utm_campaign=ip*.

Considering the very high research and development (R&D) costs and extremely long time-horizons on R&D in the bio-pharmaceutical industry, it is imperative to reverse this trend if the patent system is to continue its purpose of promoting innovative, breakthrough medical treatments that many rely on in their daily lives. This Court should direct district courts to adhere to the language of the *Mayo/Alice* test in properly considering a claim as a whole, as well as adhering to longstanding Supreme Court decisions that recognize that the § 101 inquiry is a threshold legal test that hinges upon underlying questions of fact.

CONCLUSION

Amici urge this Court to reverse the district court's decision and reaffirm that patents will continue to be available for life sciences inventions, even when they arise from discoveries of natural products or laws of nature.

Respectfully Submitted,

April 20, 2018

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APPENDIX A

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CERTIFICATE OF COMPLIANCE

1. This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 29(a)(5). The brief contains 6,080 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b).

2. This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) or Federal Rule of Appellate Procedure 28.1(e) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6). The brief has been prepared in a proportionally spaced typeface using Microsoft Word in 14 point Times New Roman font.

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CERTIFICATE OF SERVICE

I, Rose E. Olejniczak, being duly sworn according to law and being over the age of 18, upon my oath deposes and states that:

Counsel Press was retained by Kevin E. Noonan, McDonnell Boehnen Hulbert & Berghoff LLP, Counsel for *Amicus Curiae* Patent Law Scholars, to print this document. I am an employee of Counsel Press.

On April 20, 2018, Dr. Noonan authorized me to electronically file the foregoing Brief of *Amicus Curiae* Patent Law Scholars In Support of Plaintiff-Appellant and Reversal with the Clerk of the Federal Circuit using the CM/ECF System, which will serve e-mail notice of such filing on the following:

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Six paper copies will be filed with the Court within the time provided in the Court's rules.

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April 20, 2018