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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte FELIX HAUSCH, GARY GRAY,
LU SHAN, and CHAITAN KHOSLA

Appeal 2015-004105
Application 11/927,536
Technology Center 1600

Before JEFFREY N. FREDMAN, JOHN G. NEW, and
DEVON ZASTROW NEWMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal¹ under 35 U.S.C. § 134 involving a unit dose for oral administration comprising a pharmaceutical excipient and a purified plant or microbial glutenase. The Examiner rejected the claims as obvious and as not directed to patent eligible subject matter. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

¹ Appellants identify the Real Party in Interest as the Board of Trustees of the Leland Stanford Junior University (*see* App. Br. 2).

Statement of the Case

Background

“[I]ngestion of gluten, a common dietary protein present in wheat, barley and rye causes disease in sensitive individuals” (Spec. ¶ 2). “The present invention relates to the discovery that certain gluten oligopeptides [are] resistant to cleavage by gastric and pancreatic enzymes, that the presence of such peptides results in toxic effects, and that enzymatic treatment can remove such peptides and their toxic effects” (Spec. ¶ 9).

The Claims

Claims 25–29 and 45–58 are on appeal.² Claim 25 is representative and reads as follows:

25. A preparation for unit dose oral administration comprising a pharmaceutical excipient and a purified plant or microbial glutenase in dosages of 0.01 mg to 500 mg /kg body weight that when ingested by a human, is effective to cleave an ingested gluten oligopeptide having the amino acid sequence of SEQ ID NO:12 to fragments shorter than 8 amino acids.

The Issues

A. The Examiner rejected claims 25–29 and 45–58 under 35 U.S.C. § 103(a) as obvious over Robison³ (Ans. 2–7).

² We acknowledge that Appellants identify seven claim groupings (*see* App. Br. 3–4), but the arguments for them simply recite the added limitations and allege they are not found in the cited references. This is insufficient to act as a separate argument under 37 C.F.R. § 41.37. As our reviewing court held, “the Board reasonably interpreted Rule 41.37 to require more substantive arguments in an appeal brief than a mere recitation of the claim elements and a naked assertion that the corresponding elements were not found in the prior art.” *In re Lovin*, 652 F.3d 1349, 1357 (Fed. Cir. 2011).

B. The Examiner newly⁴ rejected claims 25–29 and 45–58 under 35 U.S.C. § 101 as not directed to patent eligible subject matter (Ans. 21–25).

A. *35 U.S.C. § 103(a) over Robison*

The Examiner finds that Robison teaches microbial and plant peptidases (*see* Ans. 2–4), pharmaceutical carriers for oral compositions (*see id.* at 4–5) including “ranges from about 0.001 to 30 mg/kg” (*id.* at 3) and “unitary dosages” (*id.* at 5).

The Examiner finds it obvious “to use any type of plant or microbe glutenase in an oral composition (product claimed) in Robison, because Robison expressly teach[es] the use of glutenase/enzymes of plant/microbe origin, for oral compositions” (*id.* at 5–6).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that Robison renders the claims obvious?

Findings of Fact

1. Robison teaches “administering a protein as therapy to compensate for reduced or aberrant expression or activity of the protein” (Robison 43:48–50).

2. The Specification teaches: “Glutenases of the invention include protease and peptidase enzymes having at least about 20% sequence identity

³ Robison, K., US 6,395,889 B1, issued May 28, 2002.

⁴ The newly entered § 101 rejection was properly authorized by the TC center 1600 director (*see* Ans. 26).

at the amino acid level . . . to one of the following peptidases: prolyl endopeptidase (PEP) from *F. meningosepticum*” (Spec. ¶ 31).

3. Robison teaches: “Prolyl endopeptidase (EC 3.4.21.26) (PE) (also called post-proline cleaving enzyme). PE is an enzyme that cleaves peptide bonds on the C-terminal side of prolyl residues. The sequence of PE has been obtained from . . . bacteria (*Flavobacterium meningosepticum* and *Aeromonas hydrophila*); there is a high degree of sequence conservation between these sequences.” (Robison 10:6–11).

4. Robison teaches “protein . . . can be incorporated into pharmaceutical compositions suitable for administration to a subject, e.g., a human. Such compositions typically comprise the . . . protein . . . and a pharmaceutically acceptable carrier” (Robison 57:42–49).

5. Robison teaches “a therapeutically effective amount of protein or polypeptide (i.e., an effective dosage) ranges from about 0.001 to 30 mg/kg body weight, preferably about 0.01 to 25 mg/kg body weight . . . even more preferably about 1 to 10 mg/kg” (Robison 60:10–15).

6. Robison teaches: “‘Dosage unit form’ as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier” (Robison 59:49–54).

7. Robison teaches that it “is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage” (Robison 59:47–49).

Principles of Law

“The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). “If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.” *Id.* at 417.

Analysis

We adopt the Examiner’s findings of fact and reasoning regarding the scope and content of the prior art (Ans. 2–7; FF 1–7) and agree that the claims are obvious over Robison. We address Appellants arguments below.

Appellants contend that “the art did not teach that, to detoxify gluten proteins effectively so as to reduce their immunogenicity in humans, one must select an enzyme with the ability to cleave a metastable gluten oligopeptide such as that of SEQ ID NO:12.” (App. Br. 5).

We find this argument unpersuasive because the claim is drawn to a product comprising a specific dose range for a, protease known in the prior art, not a method for detoxification of gluten. Just as in *Kao*, “the only claim element not expressly disclosed in the prior art was the previously-unknown, yet inherent, food-effect property.” *In re Huai-Hung Kao*, 639 F.3d 1057, 1072 (Fed. Cir. 2011). Here, the specific inherent property of Robison’s prolyl endopeptidase (PEP) from *F. meningosepticum* (FF 3) was that this enzyme functions as a glutenase (FF 2). “[M]erely discovering and claiming a new benefit of an old process cannot render the process again patentable.” *Kao*, 639 F.3d at 1072. *Cf. In re Wiseman*, 596 F.2d 1019,

1023 (CCPA 1979) (rejecting the notion that “a structure suggested by the prior art, and, hence, potentially in the possession of the public, is patentable . . . because it also possesses an inherent, but hitherto unknown, function which [patentees] claim to have discovered. This is not the law. A patent on such a structure would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art.”).

Appellants contend that “[e]ven if one were to select an appropriate enzyme, there is no teaching in the art of how one would select an appropriate dosage for the detoxification of gluten” (App. Br. 6).

We find this argument unpersuasive for two reasons. First, there is no requirement in the claims for detoxification of gluten in a patient, so that this argument relates to an intended use that is not even recited in the claim. However, a “mere statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable.” *In re Zierden*, 411 F.2d 1325, 1328 (CCPA 1969). Second, Robison provides specific disclosure of a preferred dose range 0.01 to 25 mg/kg body weight (FF 5) that fully falls within the range required by claim 25. *See In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003) (“In cases involving overlapping ranges, we and our predecessor court have consistently held that even a slight overlap in range establishes a *prima facie* case of obviousness.”) Here, where the ranges completely overlap, the Examiner has reasonably established the *prima facie* case of obviousness (*see* FF 5).

Appellants contend that “there is nothing in the cited art that would teach why one should select an oral formulation of an enzyme with a selected activity, in a specific dose, for oral administration” (App. Br. 6).

We are not persuaded because Robison specifically teaches that oral formulations are preferred (FF 7), that unit dose formulations are preferred (FF 6), and specifically suggests a dose range entirely overlapping with that of claim 1 (FF 5). Thus, the ordinary artisan, following Robison's suggestion to form protein therapies (FF 1) using known proteases (FF 3), would have reasonably employed the oral unit dose formulations in dose ranges suggested by Robison (FF 5–7) to achieve the oral formulation of claim 1.

Appellants contend that “Robison is a testament to the art of saying much and teaching little. The reference fails to provide any specific selection and use that would guide one of skill in the art to the specific formulations of the present claims” (App. Br. 7).

We find this argument unpersuasive because even if Robison provides a “laundry list” of proteases, the disclosure of “a multitude of effective combinations does not render any particular formulation less obvious.” *Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989). “[P]icking and choosing may be entirely proper in the making of a 103, obviousness rejection.” *In re Arkley*, 455 F.2d 586, 587 (CCPA 1972). Appellants provide no evidence of any secondary consideration to rebut the Examiner's obviousness position that the selection of known elements in known amounts from Robison would have been obvious (FF 3–7).

Appellants “submit that the dosage range is not immense, in that the claims further include the specific activity limitation regarding cleavage of a specific gluten oligopeptide. Further, Claims 51, 54 and 58 explicitly recite a much narrower dosage range: 1 to 500 mg” (App. Br. 7).

We find this argument unpersuasive because Robison teaches a preferred range of 1 to 10 mg/kg (FF 5), a smaller dose range that fully falls within the broader disclosed range required by Appellants. *Peterson*, 315 F.3d at 1329. Appellants provide no evidence of any secondary consideration with regard to the claimed dose range.

Appellants contend that “[e]ven if one were to select an appropriate enzyme, there is no teaching in the art of how one would select an appropriate dosage for the detoxification of gluten. Indeed, it is only with the findings of the present inventors that one of skill in the art would have understood the importance of metastable peptides” (App. Br. 8).

We are not persuaded because the claim is not drawn to a method of gluten detoxification, but rather to a protease composition that is rendered obvious by Robison (FF 1, 3–7). *Zierden*, 411 F.2d at 1328. Appellants provide no evidence that the claimed composition would have any property that differs from the obvious composition of Robison, in the obvious dosages taught by Robison. Unlike the facts in *Sullivan*, there are no declarations demonstrating unexpected results or showing any unexpected properties that would provide a basis for a finding of patentability despite Robison’s disclosures. *See In re Sullivan*, 498 F.3d 1345, 1353 (Fed. Cir. 2007). In addition, while the Specification discloses peptides resistant to digestion, the Specification provides only prophetic examples to show that supplementation with proteases has any physiological effect (*see* Example 3, Spec. ¶¶ 110–125, which is written in the present tense). (“[T]he examples were written in the present tense to conform with the PTO requirements on

prophetic examples.” *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1578 (Fed. Cir. 1984)).

Conclusion of Law

The evidence of record supports the Examiner’s conclusion that Robison renders the claims obvious.

B. 35 U.S.C. § 101

The Examiner finds that while the claimed invention is drawn to the eligible subject matter category of product, the claims are drawn to the judicial exception excluding patents to naturally occurring phenomena and that “neither of the two art-recognized naturally occurring products (enzymes (glutenases)) and pharmaceutical excipients) have been modified in a marked/significant way beyond that found in nature” (Ans. 22).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that the claims are not directed to patentable subject matter?

Findings of Fact

8. The Specification teaches that the “term ‘glutenase’ refers to an enzyme useful in the methods of the present invention that is capable, alone or in combination with endogenous or exogenously added enzymes, of cleaving toxic oligopeptides of gluten proteins” (Spec. ¶ 29).

9. The Specification teaches that “[c]andidate glutenases for use in the practice of the present invention can be obtained from a wide variety of sources, including libraries of *natural* and synthetic proteins” (Spec. ¶ 47; emphasis added).

10. The Specification teaches that the “glutenase proteins useful in the practice of the present invention may also be isolated and purified in accordance with conventional methods . . . from natural sources” (Spec. ¶ 60; emphasis added).

11. The Specification teaches “the term ‘unit dosage form,’ refers to physically discrete units suitable as unitary dosages for human subjects, each unit containing a predetermined quantity of glutenase in an amount calculated sufficient to produce the desired effect in association with a pharmaceutically acceptable diluent, carrier or vehicle” (Spec. ¶ 72).

12. The Examiner finds that one exemplary type of “pharmaceutical excipient” is water (*see* Ans. 22).

Principles of Law

“Laws of nature, natural phenomena, and abstract ideas’ are not patentable.” *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289, 1293 (2012) (citations omitted).

In *Chakrabarty*, scientists added four plasmids to a bacterium, which enabled it to break down various components of crude oil. . . . The Court held that the modified bacterium was patentable. It explained that the patent 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.’” . . . The *Chakrabarty* bacterium was new “with markedly different characteristics from any found in nature,” . . . due to the additional plasmids and resultant “capacity for degrading oil.”

In this case, by contrast, Myriad did not create anything. To be sure, it found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention.

Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2116–2117 (2013) (internal citations omitted).

Analysis

We adopt the Examiner's findings of fact and reasoning (Ans. 21–24; FF 8–12) and agree that the claims are not directed to patentable subject matter.

We do not find any principled difference between the claim to an isolated nucleic acid encoding the BRCA1 polypeptide in *Myriad* and the instant claim 25 drawn to an isolated glutenase enzyme with an excipient in a particular amount. *See Myriad*, 133 S. Ct. at 2113. As in *Myriad*, Appellants did not create or alter the amino acid sequence of the glutenase enzyme, and the order of the amino acids in the glutenase enzymes existed in nature before Appellants' isolated them (FF 9–10) (indeed the amino acid sequence order was disclosed in the prior art as demonstrated by Robison (FF 3)). At best, Appellants' contribution was recognizing that this natural product may have clinical uses in certain patient populations (*see* Spec. ¶ 9). However, the claims are not drawn to methods of treatment of particular conditions in particular patient populations using a glutenase enzyme composition, but rather are drawn to the glutenase enzyme product itself.

Like *Myriad* and *Funk Brothers*, and unlike *Chakrabarty*, the glutenase enzyme of claim 25 was not a creation of Appellants, but rather a product of nature. And there is nothing markedly different between the glutenase enzyme of claim 25 and the natural product other than that Appellants have purified the enzyme and mixed it with water (FF 9–12). But separating the protein from the cell is not an act of invention. *See*

Myriad, 133 S.Ct. at 2117; *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 132 (1948); *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980).

Appellants contend that the claims do

not read on any naturally occurring substance, and, to the extent that one can use a naturally occurring glutenase or pharmaceutical excipient to form the preparation, the claim, as a whole, recites a product that has markedly different characteristics from any naturally occurring substance. More importantly, the recitation of the amount of the purified glutenase as determined by the weight of a subject intended to consume a unit dose form of it, and its properties when ingested, renders the claimed subject matter markedly different in function and properties from any naturally occurring source of a glutenase or pharmaceutical excipient.

(Reply Br. 3).

We do not find this argument persuasive. Claim 25 is drawn to a composition comprising a particular amount of a glutenase enzyme in purified form and an excipient, where the excipient may be water (FF 12). Because *Myriad* expressly teaches that purification “is not an act of invention” *Myriad*, 133 S. Ct. at 2117, the only difference that might be present between any purified prior art glutenase enzyme and the claim is the amount of enzyme present. We do not agree with Appellants that the selection of a particular amount of glutenase enzyme in aqueous solution renders the composition markedly different from the same glutenase enzyme in aqueous solution that is in higher or lower amounts. And the Specification clearly identifies the glutenase enzyme as a natural product (FF 9–10).

If the amount of a naturally occurring product alone was sufficient to render the composition markedly different, then Myriad could have simply recited a requirement for an amount of nucleic acid sufficient to permit polymerase chain detection of breast cancer to avoid the patentable subject matter issue, a result we think stands in opposition to the position of the Supreme Court. Indeed, a logical extension of Appellants' position would allow a patent on thirty pieces of purified silver, if that were a novel and unobvious amount determined to be the particular value of purified currency necessary to induce betrayal.

Appellants also contend:

This claim does not “tie up” the natural product, i.e. glutenases having the stated biological effect. The art is free to use such glutenases in non-purified form, in dosages containing amounts outside of those recited, for any purpose not requiring oral administration to a human, and for any preparation not suitable for oral administration, and so forth.

(Reply Br. 4).

We do not find this argument persuasive. Because the claims are open to any human, who may weigh anywhere between about 260 g at birth to about 442 kg in body weight, claim 25 broadly encompasses any aqueous composition comprising between 0.0026 mg and 221,000 mg. This broad range reasonably ties up a very significant number of enzymes at a very wide range of amounts for a number of purposes. Because the claim is to a product, not a process, there is no constraint on the purpose for which the product is being used.

Appellants then address twelve factors identified in *The Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving*

Laws of Nature, Natural Phenomena, & Natural Products (Guidance), dated March 4, 2014, and contend that the factors weighing toward eligibility are satisfied or not relevant, and that the factors weighing against eligibility are not satisfied (*see* App. Br. 5–8). We do not specifically address these factors because they simply attempt to summarize *Myriad*, and address the issue of whether the natural product at issue satisfies *Myriad*'s test of a product that is “markedly different” from the natural product. *Myriad*, 133 S. Ct. at 2117. We have already determined that the claimed glutenase enzyme and water product is not markedly different by virtue of the selection of a particular dose range.

Indeed, in the most recent USPTO guidance in the May 6, 2016, update, *Subject Matter Eligibility Examples: Life Sciences*, the guidance provides an example regarding vaccines with an example claim drawn to: “A vaccine comprising: Peptide F; and a pharmaceutically acceptable carrier” where peptide F is a naturally occurring protein isolated from a virus (Subject Matter Eligibility Examples at pages 2–3). The guidance states that “mixing the peptide with a carrier such as water does not markedly change the characteristics of either component, because each component continues to have the same properties in the mixture as it had alone” and concludes that the “claim does not qualify as eligible subject matter” (Subject Matter Eligibility Examples at page 5).

Conclusion of Law

The evidence of record supports the Examiner's conclusion that the claims are not directed to patentable subject matter.

SUMMARY

In summary, we affirm the rejection of claim 25 under 35 U.S.C. § 103(a) as obvious over Robison. Claims 26–29 and 45–58 fall with claim 25. 37 C.F.R. § 41.37(c)(1)(iv)

We affirm the rejection of claim 25 under 35 U.S.C. § 101 as not directed to patent eligible subject matter. Claims 26–29 and 45–58 fall with claim 25. 37 C.F.R. § 41.37(c)(1)(iv)

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED