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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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Ex parte JEFFREY DANIEL HILLMAN, ERIC W.T. CHOJNICKI, and RAVI SHANKAR

_____

Appeal 2018-002804
Application 11/265,414[1]
Technology Center 1600

_____

Before DONALD E. ADAMS, RACHEL H. TOWNSEND, and MICHAEL A. VALEK, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of administering a high glycine diet to overweight or obese animals in order to reduce white adipose tissue in the overweight or obese animal, induce apoptosis in white adipocytes in the overweight or obese animal, or produce weight loss in the overweight or obese animal, which have been rejected as failing to comply with the written description requirement, or failing to further limit the subject matter of the claim upon which they depend and/or

[1] We use the word "Appellant" to refer to "Applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as LPThera, LLC. (Appeal Br. 1.)

as being indefinite and obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm-in-part.

STATEMENT OF THE CASE

Appellant's Specification indicates that "[i]n the United States it is estimated that 60% of adults meet the clinical requirements to be considered overweight or clinically obese resulting in 300,000 deaths annually." (Spec. ¶ 2.) "[T]here is a great deal of interest in the development of a pharmaceutical approach" to prevent and/or decrease "the incidence and prevalence of individuals that are overweight or clinically obese." (*Id.*) "The pharmaceutical approach is attractive since there is a strong likelihood of greater compliance due to the probable ease of application and use." (*Id.*) Appellant's claims are directed to such a pharmaceutical approach.

Claims 1–4, 8–11, 19–22, and 24–31 are on appeal.[2] Claims 1, 3, and 8 are representative and read as follows:

> 1. A method for reducing white adipose tissue in an overweight or obese animal comprising administering a high glycine diet comprising 10% to 30% glycine by weight of the diet to the animal, wherein white adipose tissue in the overweight or obese animal is reduced.
>
> 3. A method for inducing apoptosis in white adipocytes of an overweight or obese animal comprising administering a high glycine diet comprising 10% to 30% glycine by weight of the diet to the overweight or obese animal, wherein apoptosis in the overweight or obese animal is induced.

[2] Claims 13, 14, 17, and 18 remain pending but are withdrawn from consideration as being directed to non-elected subject matter. (Appeal Br. 1.)

> 8. A method for producing weight loss in an overweight or obese animal comprising administering a high glycine diet comprising 10% to 30% glycine by weight of the diet to the overweight or obese animal, wherein weight loss in the overweight or obese animal is produced.

(Appeal Br. 36–38.)

The prior art relied upon by the Examiner is:

Name	Reference	Date
McLean	US 5,484,623	Jan. 16, 1996
McCarty	US 5,914,326	June 22, 1999
Yuan	US 2002/0136785 A1	Sept. 26, 2002
Abe	US 2004/0235923 A1[3]	Nov. 25, 2004
Kelley, *The Lipotropic Effect of Folic Acid on Rats Receiving Various Purified Diets*, 187(2) J. Biol. Chem. 529–535 (1950)		
Kalman, *The Effects of Pyruvate Supplementation on Body Composition in Overweight Individuals*, 15(5) J. Nutrition 337–40 (1999)		
Swendseid, *Ratios of Essential-to-Nonessential Amino Acids in Plasma from Rats Fed Different Kinds and Amounts of Proteins and Amino Acids*, 80 J. Nutrition 99–102 (1963)		
Sullivan, *Studies on the Biochemistry of Sulphur*, 47(2) Public Health Reports 75–83 (1932)		

The following grounds of rejection by the Examiner are before us on review:

A. Claims 26 and 27 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement

[3] The Examiner relies on this published national phase version of Abe as the English language equivalent of the published PCT application WO 2002/100193, which is in Japanese. However, the Examiner relies on the publication date of the earlier published PCT version of Abe.

B. Claim 30 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement

C. Claims 1–4, 8–11, 19–22, and 24–31 under 35 U.S.C. § 112, second paragraph as being indefinite

D. Claims 20 and 21 under 35 U.S.C. § 112, second paragraph as being indefinite

E. Claim 26 and 27 under 35 U.S.C. § 112, second paragraph as being indefinite

F. Claims 2, 4, and 10 under 35 U.S.C. § 112, fourth paragraph as failing to further limit the subject matter of the claim upon which they depend

G. Claims 1–4, 8–10, 19–22, and 24–31 under 35 U.S.C. § 103(a) as unpatentable over Kelley, McCarty, Kalman, and Yuan

H. Claims 11, 20, and 21 under 35 U.S.C. § 103(a) as unpatentable over Kelley, McCarty, Kalman, Yuan, and McLean

I. Claims 24, 25, 28, and 29 under 35 U.S.C. § 103(a) as unpatentable over Kelley, McCarty, Kalman, Yuan, and Swenseid

J. Claims 1–4, 8–10, 19, 22, 26, 27, and 29–31 under 35 U.S.C. § 103(a) as unpatentable over Sullivan, McCarty, Kalman, and Yuan

K. Claims 11, 20, and 21 under 35 U.S.C. § 103(a) as unpatentable over Sullivan, McCarty, Kalman, Yuan, and McLean

L. Claims 19, 24, 25, and 28under 35 U.S.C. § 103(a) as unpatentable over Sullivan, McCarty, Kalman, Yuan, and Swenseid

M. Claims 1–4, 8–10, 22, 24–27, and 29–31 under 35 U.S.C. § 103(a) as unpatentable over Abe, McCarty, Kalman, and Yuan

N. Claims 11, 20, and 21 under 35 U.S.C. § 103(a) as unpatentable over Abe, McCarty, Kalman, Yuan, and McLean

O. Claims 24, 25, 28, and 29 under 35 U.S.C. § 103(a) as unpatentable over Abe, McCarty, Kalman, Yuan, and Swenseid.

DISCUSSION

Rejections Not Based on Prior Art

A. Claims 26 and 27: Written Description and Indefiniteness

Claims 26 and 27 have been rejected by the Examiner under 35 U.S.C. 112, first paragraph as containing new matter because the Examiner concludes there is not support for the phrase "normal recommended diet." (Non-Final Action[4] 4.) The Examiner finds that this language requires a diet that is normal and that this "normal diet" be recommended. (Ans. 22.) The Examiner notes that a "supplemented diet" and a "non-supplemented diet" are "discussed extensively" in the Specification, and that the Specification discloses low-fat diet, low-calorie diet, and low-carbohydrate diet "in the context of a normal recommended diet that is reduced in fat, calorie or carbohydrates." (Non-Final Action 4.) However, explains the Examiner, claims 26 and 27 are not limited to a low-fat, low-calorie, or low-carbohydrate diet. (*Id.*)

The Examiner also rejects these claims as being indefinite because "[t]he specification does not define what a 'normal recommended diet' is for an animal." (*Id.* at 8.) The Examiner recognizes that low-fat, low-calorie,

[4] The Non-Final Action from which Appellant takes its present Appeal is dated November 28, 2016.

and low-carbohydrate diets are defined, but the Specification does not specify "where the recommended amounts come from or how the recommended values [are] determined" and the limitation "normal recommended diet" in these claims "does not define recommended in relation to these specific characteristics" of fat, calorie, or carbohydrate. (*Id.*)

Appellant argues that claims 26 and 27 do not encompass new matter and are definite because the Specification "teaches the supplementation of low-fat diets, low calorie diets, low carbohydrate diets (see paragraphs [0080]-[0082] in relation to normal recommended diets." (Appeal Br. 7.) Appellant also contends that normal recommended diets are disclosed in working Example 1 and paragraph 111. (*Id.*)

We find the Examiner has the better position on both lack of written description and indefiniteness.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail so that it "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed Cir. 2010) (en banc). Although it is true that "the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue," the disclosure, nevertheless, must convey with reasonable clarity to one of ordinary skill in the art that the inventor was in possession of the invention that is claimed. *Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000).

35 U.S.C. § 112, second paragraph requires claims, when read in light of the specification, to inform with reasonable certainty those skilled in the

art about the scope of the invention. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 910 (2014). Thus, a claim is indefinite when it contains words or phrases whose meaning is unclear. *In re Packard*, 751 F.3d 1307, 1310–13 (Fed. Cir. 2014) (noting that "It is the claims that notify the public of what is within the protections of the patent, and what is not."); *see also Ex parte McAward,* 2017 WL 3669566, at *5 (PTAB Aug. 25, 2017) (precedential) (explaining that the USPTO considers a claim indefinite when it "contains words or phrases whose meaning is unclear").

Claim 27 requires that in the method of claim 1 for producing weight loss in an overweight or obese animal, the animal is administered a high glycine diet which "supplements a normal recommended diet for the animal." Claim 26 is similar, though the high glycine diet which "supplements a normal recommended diet" is administered to achieve reduction of adipose tissue.

We agree with Appellant (Appeal Br. 7) that the Specification discusses the supplementation of low-fat diets, low calorie diets, low carbohydrate diets with a high glycine diet for producing weight loss in overweight or obese animals. (*See* Specification ¶¶ 78–82[5].) However, what constitutes one of those diets is defined with respect to a lower percentage of fat, calories, or carbohydrates as compared to "the normal recommended amount" in a diet for "a given species of a given age, weight, and general health condition." (Spec. ¶¶ 80–82.) And, the Specification does not provide a person of ordinary skill in the art with a basis for what

[5] We refer to the paragraphing in the published application, US 2006/0093650 A1, published May 4, 2006.

constitutes a normal recommended amount of those components. The Specification describes that a "[n]ormal diet is a diet that is not supplemented with glycine, but contains normal amounts of glycine." (*Id.* ¶ 74.)

Additionally, the Specification does not provide what objective standard is to be consulted to select a normal recommended diet for any animal.

Appellant refers to Example 1 as disclosing a "normal recommended diet." (Appeal Br. 7.) Although Example 1 provides the name and content of a commercially available diet for rats, there is nothing in the Specification to indicate whether this is a normal recommended diet for rats or is a low-fat, low-carbohydrate, or low-calorie diet for rats. The Specification merely states that the commercial product "has about 1-2% glycine present in the lactalbumin component and is considered a non-supplemented diet." (Spec. ¶ 90.)

Paragraph 111 of the Specification, also referred to by Appellant (Appeal Br. 7), does not provide such clarity. There it is simply noted that in the "preliminary studies, glycine was administered orally as part of the normal diet of the test animals." (Spec. ¶ 111.) There is again nothing in this paragraph to indicate whether "the normal diet" that was administered was a normal recommended diet for rats or was a low-fat, low-carbohydrate, or low-calorie diet for rats that is a normal recommended diet for an obese or overweight rat.

In short, Appellant's argument in the brief that the invention recited in these claims are described and definite is not supported by the evidence. *Johnston v. IVAC Corp.*, 885 F.2d 1574, 1581 (Fed. Cir. 1989) ("Attorneys'

argument is no substitute for evidence.") Consequently, we agree with the Examiner that the Specification does not reasonably convey to one of ordinary skill in the art that Appellant was in possession of the invention of Claim 26 or 27 requiring that in the method of claim 1 or 8, the animal is administered a high glycine diet which "supplements a normal recommended diet for the animal."

Furthermore, for these very same reasons, we find the scope of claims 26 and 27 ambiguous in defining the claimed invention.[6]

In view of the foregoing, we affirm the Examiner's rejection of Claims 26 and 27 under (1) 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement, and (2) 35 U.S.C. § 112, second paragraph as being indefinite.

B. Claims 20 and 21: Indefiniteness

The Examiner considers claims 20 and 21 to be indefinite for similar reasons that claims 26 and 27 were considered to be indefinite, namely that the baseline "normal recommended amount" of fats, calories, or carbohydrates can vary depending on the source of the recommendation. (Non-Final Action 7.) Appellant argues that because the terms "low-fat," "low carbohydrate," and "low calorie" are defined in the Specification "those skilled in the art are clearly informed about the scope of the invention with reasonable certainty." (Appeal Br. 6.)

However, for the reasons just addressed above, we find the definition provided in the Specification for "low-fat," "low carbohydrate," and "low

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[6] The Examiner points out additional issues that he considers render these claims indefinite. (Non-Final Action 8.) We do not agree with these other contentions by the Examiner. *See* Section D., *infra*.

calorie" diets (Spec. ¶¶ 80–82) does not provide a person of ordinary skill in the art with a basis for what constitutes a normal recommended amount of fat, calories, or carbohydrates, nor does the Specification provide what objective standard is to be consulted to select a normal recommended diet for any animal.

Thus, we agree with the Examiner that the scope of claims 20 and 21 are ambiguous, and for this reason we affirm the Examiner's rejection of these claims under 35 U.S.C. § 112, second paragraph as being indefinite.

C. Claim 30: Written Description

Claim 30 has been rejected by the Examiner under 35 U.S.C. 112, first paragraph as containing new matter because the Examiner concludes there is no support for the requirement that the method does not cause any "deleterious side effects." (Non-Final Action 5.) The Examiner finds that the Specification only describes no deleterious side effects were observed "during prolonged administration" of optimal and super-optimal doses of glycine without indicating what percentage of glycine those doses included. (*Id.* (referring to Spec. ¶ 45).) Moreover, the Examiner notes that the claim does not include a time frame and the Specification only provides for what was observed over a prolonged administration. (*Id.*) The Examiner further states that an observation is "different" than an assessment of whether a deleterious side effect was "caused" by the method, which is the claimed issue. (*Id.*)

We disagree with the Examiner's conclusion regarding claim 30. We conclude that the Specification's teaching at paragraph 45 that deleterious side-effects were not observed is a sufficient proxy for observable deleterious side-effects not being caused, as demonstrated by Example 6 of

the Specification. In Example 6, it is disclosed that, after feeding a diet of 15% glycine and 85% TD80406, "[n]o gross lesions or treatment related abnormalities other than weight were reported at necropsy of animals fed," "[n]o differences in blood chemistry and complete blood counts were observed" compared to control animals, and "no microscopic changes from normal histology" were observed. (Spec. ¶ 100.) In short, weight difference was a reported difference from normal but nothing else was reported deficient compared to normal. Thus, we conclude that the Specification reasonably conveys to one of ordinary skill in the art that the inventor had possession of a method of producing weight loss comprising administering a high glycine diet comprising 10 to 30% glycine by weight of the diet where no deleterious side effects were caused.

Consequently, we reverse the Examiner's rejection of claim 30 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

D. Claims 1–4, 8–11, 19–22, and 24–31: Indefiniteness

The Examiner rejects claims 1–4, 8–11, 19–22, and 24–31 as a group under 35 U.S.C. § 112, second paragraph as being indefinite "because without a time frame [recited] for [carrying out] the method, what constitutes the diet (used as the basis of the glycine content calculation) is not clear." (Non-Final Action 6.) That is the Examiner is unclear whether a "single snack with a large amount of glycine or a glycine dietary supplement may fall within the scope of the claims." (*Id.*)

Furthermore, the Examiner contends that without a recited time frame for carrying out the method, it is unclear how much of a reduction in the various methods must be produced. (*Id.*)

We disagree with the Examiner's conclusion. We agree with the Examiner that the claims are broad in what may constitute the "diet" of the animal in the methods in which "a high glycine diet" is to be administered as well as for how long the diet must be administered. However, "breadth is not to be equated with indefiniteness." *In re Miller*, 441 F.2d 689, 693 (CCPA 1971). The test for definiteness under the second paragraph of 35 U.S.C. § 112 is: "whether those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576 (Fed. Cir. 1986).

The claims are clear in reciting that whatever the "diet" is that the animal is administered, it must include 10–30% by weight glycine and that a reduction of white adipose tissue is achieved (claim 1), or inducing apoptosis in which adipocytes is achieved (claim 3), or weight loss is achieved (claim 8). At least one example is provided (Example 1) in which a diet that has 10–30% by weight glycine is provided to an animal and for a time period in which weight loss was observed as compared to a control animal who was provided with a diet that only had 1–2% by weight glycine. In light of this, we determine that one of ordinary skill in the art knows how to determine when a diet includes 10–30% by weight glycine and when an animal who has been administered such a diet has achieved weight reduction.

Appellant also points to additional description in the Specification illustrating that it was known how to measure the end-points of independent claims 1 and 3. (*See* Appeal Br. 5.) Thus, we determine that one of ordinary skill in the art knows how to determine when the end point required by each of the claims have been reached with reasonable certainty. Consequently,

when the claim language is construed in light of the Specification, we conclude that the person having ordinary skill in the art would have understood its meaning, despite the breadth of the claims in not identifying a specific time frame for carrying out the method to achieve a specified result or identifying how the glycine that is 10-30% of the diet should be provided, (e.g., as a snack or as a supplement or something else), in the method to achieve the specified result.

In view of the foregoing, we reverse the Examiner's rejection of claims 1–4, 8–11, 19–22, and 24–31 under 35 U.S.C. § 112, second paragraph as being indefinite.

E. Claims 2, 4, 10: Failure to Further Limit

The Examiner rejects claims 2, 4, and 10 under 35 U.S.C. 112, fourth paragraph finding that these claims fail to further limit the claims from which they depend, *i.e.*, 1, 3, and 8, respectively, which require "administering a high glycine diet comprising 10% to 30% glycine." (Non-Final Action 9.) The Examiner explains that "[g]lycine is understood in the art to be a specific compound," not a genus of multiple compounds (*id.*) and no alternative definition of glycine is provided in Appellant's Specification (Ans. 9). The Examiner notes that claims 2, 4, and 10, which recite that "the high glycine diet comprises" molecules of Formula I, II, or III does not further limit the glycine required by the diet of claims 1, 3, and 8 because only the one formulation of Formula II where R1=R2=H is glycine and the remaining formulations encompassed within Formulae I, II, and III "do not fall within the scope of the 'glycine' as would be defined by the person of ordinary skill in the art." (Non-Final Action 9; Ans. 9.)

We agree with the Examiner's factual findings and conclusion that claims 2, 4, and 10 fail to further limit the subject matter of the claims from which they depend. Appellant's sole substantive response to this rejection[7], is a mere assertion, without more, that "[d]ependent claims 2, 4, and 10 modify the 'high glycine diet' element of claims 1, 3, and 8, respectively." (Appeal Br. 6.) Although we agree with Appellant that such is the attempt of the dependent claims, we disagree that the claims properly further modify claims 1, 3, and 8. As the Examiner explained, claims 1, 3, and 8 require administration of a "high glycine diet" and glycine would be understood to mean the amino acid with the following chemical formula NH_2-CH_2-COOH. Formulas I–III allow for numerous compounds that are not NH_2-CH_2-COOH. Thus, the scope of claims 2, 4, and 10 broaden the scope of the high glycine diet required by claims 1, 3, and 8 to be administered, not further limit that diet.

Thus, we affirm the Examiner's rejection of claims 2, 4, and 10 under 35 U.S.C. § 112, fourth paragraph.

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[7] Appellant also objects to the timeliness of the Examiner's rejection. (Appeal Br. 6.) "The goal of examination is to clearly articulate any rejection *early* in the prosecution process" MPEP 706 (emphasis added). However, so long as the applicant "has the opportunity to provide evidence of patentability and otherwise reply completely at the earliest opportunity" (*id.*), there is no appealable issue for us to consider concerning the timing as to the Examiner's rejection. The Examiner issued the rejection of claims 2, 4, and 10 under 35 U.S.C. 112, fourth paragraph in an Office Action that was not made final. It was Appellant's choice to file the present Appeal of the Examiner's Non-Final Office Action, rather than continue prosecution before the Examiner. We do not find that Appellant has been precluded from responding timely or completely to the Examiner's rejection.

II

Prior Art Based Rejections

A. The Kelley based rejections

The Examiner finds that Kelley discloses administering a diet that contains 10% glycine to weanling rats. (Non-Final Action 15.) The Examiner further finds that, although the rats are not overweight or obese, Kelley discloses that the rats fed a diet supplemented with 10% glycine diet had a reduced weight gain compared to weanling rats who were fed a diet that was not so supplemented. (*Id.* (referring to Kelley Table 1).)

The Examiner finds that McCarty discloses a method for promoting weight and fat loss by administering a composition that includes hydroxycitrate, carnitine, and an agent that promotes rapid intramitochondrial generation of oxaloacetate or induces endogenous production of pyruvate. (*Id.* at 16.) The Examiner finds that McCarty discloses that glycine is an agent that promotes rapid intramitochondrial generation of oxaloacetate and can serve as a pyruvate precursor. (*Id.* (citing McCarty 3:18–32 and claim 6).)

The Examiner further finds that Kalman teaches pyruvate supplementation decreases body weight, body fat, and percent body fat. (*Id.*)

The Examiner relies on Yuan for its disclosure that it was known to administer compositions to animals such as humans, rats or dogs to treat type 2 diabetes or obesity where the composition acts to increase body weight loss by an increase in energy expenditure and/or a decrease in food intake. (*Id.*)

In light of the foregoing, the Examiner concludes that it would have been obvious to one having ordinary skill in the art to administer a diet with 10% glycine to overweight or obese animals, including humans or dogs with a reasonable expectation that the obese animal would have a reduced weight gain. (*Id.* at 16–17.) According to the Examiner, "[w]hen the same diet is administered to the same population, the same results must necessarily occur, whether that be reducing white adipose tissue, inducing apoptosis in white adipose tissue, reducing white adipose cell size, producing weight loss by reducing fat content or the absence of deleterious side effects." (*Id.* at 17.)

We disagree with the Examiner's findings with respect to McCarty and the conclusion of obviousness.

Appellant argues that the reduction in weight gain of an immature animal such as was involved in the experimentation in Kelley is a different biological effect than the loss of weight by an overweight or obese animal and that the Office has not provided any evidentiary showing that the two can be correlated. (Appeal Br. 10–11.) Appellant further argues that "Kelley presented experiments with several variables other than glycine which could account for the lower weight gain." (*Id.* at 9.) Appellant provides the Declaration of Dr. Joy A. Cavagnaro[8] in support of the foregoing. (*Id.* at 7–9; Cavagnaro Declaration ¶¶ 3–8.) Dr. Cavagnaro has experience in regulatory affairs and product development in the areas of "vaccines, cellular and gene therapies, animal-based and plant-based biotherapeutics, biotechnology-derived and tissue engineered products"

[8] This Declaration is dated October 7, 2015.

garnered from working in industry, academia, and at the FDA Center for Biologics Evaluation and Research. (Cavagnaro Declaration ¶ 1.) Dr. Cavagnaro explains with respect to Kelley that (1) there is no data on the amount of food consumed between groups, (2) the diet supplemented with glycine had a concomitant reduction in carbohydrate content, (3) the addition of folic acid with the 10% glycine supplementation corrected the reduced weight gain as compared to the experimental group fed a diet with 10% glycine supplementation, and (4) further reducing the carbohydrate content (in the 10% glycine and 4% RNA experiment) resulted in further reduction in weight gain compared to the experimental group fed a diet with 10% glycine supplementation. (*Id.* ¶¶ 5–7.) Dr. Cavagnaro notes that "because the Kelley study was not intended to investigate weight effects, key data for assigning reduced weight gain to any variable are not reported or missing." (*Id.* ¶ 4.) Dr. Cavagnaro asserts that the data of Kelley demonstrates that "the limited folic acid in the diet is playing a significant role in weanling rat growth" and that "it appears to play a key role . . . in weanling rats reduced weight gain." (*Id.* ¶ 7.) She further asserts that one cannot ascribe the initial drop in weight gain seen in the 10% glycine supplemented experimental group to reduced sucrose (which was removed and replaced with glycine and RNA), amount of food consumed (which was not recorded across any of the groups), or glycine because the further reduction in weight gain from 114 g in the experimental group that was supplemented with 10% glycine to 99g in the experimental group that was supplemented with 10% glycine and 4% RNA could not have been due to glycine given that the glycine percentages were the same in both groups. (*Id.* ¶ 6.) Dr. Cavagnaro concludes that one of ordinary skill in the art would

not have expected, from the teachings of Kelley, "to make modifications and expect success in using glycine on overweight or obese animals with necessarily a different basal nutritional/amino acid/energy requirement" than the weanling male rats used in the experiments of Kelley. (*Id.* ¶ 8.)

Although we agree with Appellant that Kelley was not intended to study weight effects, there is no doubt that Kelley's data establishes that the rats fed a diet that included 10% glycine gained less weight than rats fed a diet that did not include 10% glycine. (Kelley 530 (Table 1).) Certainly the addition of folic acid corrected some of the reduction observed with only 10% glycine supplementation, but even where folic acid was administered, along with 10% glycine, the rats gained less weight than rats fed a diet that did not include 10% glycine. Although those rats also received a lower amount of carbohydrates than the non-glycine-supplemented group, the glycine-supplemented group received a "high glycine" diet, as required by Appellant's claims, and when administered that diet, had a reduced weight gain compared to those rats not provided with a high-glycine diet.

Despite the foregoing, we do agree with Appellant that the Examiner has not established, in the absence of hindsight, a prima facie case of obviousness of the claimed method. At a minimum, we agree with the Examiner that neither Kelley nor any of the other references relied upon would have provided one of ordinary skill in the art with a reasonable expectation of success of producing weight loss in overweight or obese animals by administering a high glycine diet (Appeal Br. 12) as required by claim 8 (or of reducing white adipose tissue as required by claim 1 or of inducing apoptosis in white adipocytes as required by claim 3).

First, Kelley teaches nothing with respect to weight loss. At most it provides data regarding the lack of weight gain. Moreover, although we agree with the Examiner that rats fed a diet that included 10% glycine gained less weight than rats fed a diet that did not include 10% glycine, we find Dr. Cavagnaro's discussion that it is not clear from Kelley that the reduction in weight is due solely to the administration of 10% glycine to be persuasive. (Cavagnaro Declaration ¶¶ 5–7)

Additionally, we agree with Appellant that the Examiner has not established that the non-overweight, immature rat growth model is a recognized, or even a reasonable, animal model for overweight or obese animals. (Appeal Br. 11.) As Dr. Cavagnaro notes, overweight/obese rats have different metabolic needs and are in a different growth state than weanling rats. (*See, e.g.*, Cavagnaro Declaration ¶¶ 7, 17.)

Furthermore, although McCarty is directed at a method for promoting weight and fat loss, as Appellant explains, McCarty does not indicate "that the agent that promotes the rapid intramitochondrial generation of oxaloacetate *could be used alone* to promote fat or weight loss and instead teaches that [agent] is used to synergize the active ingredients [the known diet aids, hydroxycitrate and carnitine]." (Appeal Br. 12*;* McCarty 1:6–9 ("the invention relates to coadministration of hydroxycitrate, carnitine and a compound which increases mitochondrial synthesis of oxaloacetate."), *see also id.* 2:53–57.) Thus, although glycine is noted in McCarty to be a compound that promotes the rapid intramitochondrial generation of oxaloacetate (*id.* 3:17–22), that teaching does not provide a reason why one of ordinary skill in the art would have reasonably expected administration of a high glycine diet where hydroxycitrate and carnitine are not also being

added, to produce weight loss in any type of animal, much less one that is obese or overweight.

As Appellant further notes, McCarty does not teach that glycine can enhance the endogenous generation of pyruvate, but rather, indicates that metformin and biotin are such compounds. (Appeal Br. 13; McCarty 3:44–54.) Thus, even if it were the case that pyruvate supplementation were known to decrease body weight, body fat, and percent body weight, as the Examiner contends, McCarty does not provide any teaching relevant to the relationship of glycine to the generation of pyruvate.

Furthermore, Kalman does not concern the effects of administration of glycine to obese patients, only that pyruvate supplementation "results in a modest, but significant, decrease in body weight and body fat." (Kalman 349.)[9] Indeed, the study in Kalman was directed at determining whether lower doses of pyruvate could have a positive effect on exercise performance and body composition in an overweight but healthy population. (Kalman 338.) Finally, Appellant explains that Yuan says nothing with respect to glycine. (Appeal Br. 13.)

Appellant explains why from a scientific standpoint that the addition of glycine in one's diet does not equate to an increase in pyruvate. (*Id.*) Appellant explains that enzymes are required to convert that glycine first to

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[9] We disagree with Appellant (Appeal Br. 12) that Kalman does not suggest that pyruvate alone when administered to an obese patient would likely contribute to weight loss. (*See* Kalman 339 ("Thus, the weight and fat loss incurred in the experimental group ostensibly would be due to the supplementation of pyruvate alone . . . [o]ur data would suggest that circuit training at a frequency of 3x/wk for a 6 wk duration is inadequate at inducing a weight or body fat loss.").)

serine and then from serine to pyruvate and the prior art cited by the Examiner does not teach or suggest that addition of glycine would necessarily result in an increase in pyruvate. (*Id.*) We agree that there is a lack of evidence by the Examiner on this record that one of ordinary skill in the art would have reasonably expected administering a high glycine diet to any animal would have resulted in an increase in that animal's pyruvate levels, much less one that would reasonably have been expected to have an effect on reducing body fat or body weight.

The Examiner's assertion in the Answer, that a "person of ordinary skill in the art would have been motivated to administer the high glycine composition of the primary reference[, i.e., Kelley,] to overweight or obese animals to at least slow weight gain" which is "a feature that was explicitly disclosed by the applied prior art" albeit in the different patient population of Kelley (Ans. 28–29), ignores that the prior art cited by the Examiner does not establish that the model of Kelley would be indicative of what one of ordinary skill in the art would reasonably expect to happen in an overweight or obese population with "a different basal nutritional/amino acid/energy requirement." (*See* Cavagnaro Decl. ¶ 8; *see also* Reply Br. 9.) The Examiner asserts that Appellant "fails to suggest that the different patients are critical to the effects of administration of a high glycine diet." (Ans. 29.) We disagree. Appellant's expert Dr. Cavagnaro provides testimony in that regard, i.e., obese or overweight populations have different "basal nutritional/amino acid/energy requirement." (Cavagnaro Decl. ¶ 8; *see also id.* ¶ 7.)

We agree with Appellant (Appeal Br. 16) that the Examiner has failed to establish a reason with a rational underpinning that one of ordinary skill in

the art would have been motivated to administer the 10% glycine diet of Kelley to obese or overweight animals with a reasonable expectation of producing weight loss. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). As just discussed, the Examiner has failed to establish by a preponderance of the evidence that one of ordinary skill in the art would have even expected to slow weight gain in an obese or overweight population by administering the 10% glycine diet of Kelley. Whether weight loss would have been inherent if the diet of 10% glycine supplemented basal diet of Kelley were administered to an obese or overweight population of animals does not overcome the requirement of establishing a reason to administer the diet to the claimed population in the first instance. As Appellant explains, this is a method step that must be taught or suggested by the prior art. (Appeal Br. 11.) We find the Examiner's rejection lacking in this regard.

The Examiner's reliance on additional prior art to address dependent claims does not address the foregoing deficiency. For example, Swendseid reports results of an experiment on weanling rats and young adult male rats where the ratio of essential and nonessential amino acids was determined and the average weight gain was observed. (Swendseid 99–100.) Supplementing with an 18% casein diet with 7.5% glycine "caused a slight reduction if growth rate (group 8) and a law plasma EN[10] ratio" in the weanling rats. (*Id.* at 100.) Similar results were observed in the young adult male rats. (*Id.* at 100 (Table 2).) Despite the fact that Swendseid "showed that administration of the same diet to weanling rats and young adult rats had the same effects"

[10] EN ratio is the ratio of essential-to-nonessential amino acids. (*Id.* at 99.)

(Ans. 29), Swendseid does not add any evidence as to what would or would not be expected by one of ordinary skill in the art with respect to overweight or obese animals. (*See also* Cavagnaro Declaration ¶ 15.)

McLean does not relate to glycine in the diets of animals, but rather to a dietary system to combat obesity which system comprises a two part regimen. (*See, e.g.*, McLean 6:61–7:4.) Part one of the regimen is ingestion of "prescribed foods that include low saturated fat, low carbohydrate, moderate protein foods and oils high in monounsaturates and certain fatty acids" and part two is ingestion of "a variety of supplements including vitamins and minerals." (*Id.*)

Thus, for the foregoing reasons, we reverse the Examiner's rejection of:

(i) Claims 1–4, 8–10, 19–22, and 24–31 under 35 U.S.C. § 103(a) as unpatentable over Kelley, McCarty, Kalman, and Yuan,

(ii) Claims 11, 20, and 21 under 35 U.S.C. § 103(a) as unpatentable over Kelley, McCarty, Kalman, Yuan, and McLean; and

(iii) Claims 24, 25, 28, and 29 under 35 U.S.C. § 103(a) as unpatentable over Kelley, McCarty, Kalman, Yuan, and Swenseid.

B. The Sullivan based rejections

The Examiner's rejection of the claims relying on the teachings of Sullivan is much the same as the rejection relying on Kelley. In this rejection, the Examiner finds that Sullivan discloses administering a diet that contains 10% glycine (10 g of glycine replacing 10 g of corn starch "per 100g of basal diet") to rats that were 27–31 days old. (Non-Final Action 22.) The Examiner further finds that, although the rats were not overweight

or obese, Sullivan discloses that the rats fed a diet supplemented with 10% glycine diet "lost 6 to 9 grams within a two week time frame." (*Id.*) The Examiner relies on McCarty, Kalman, and Yuan as described above in the Kelley based rejection to conclude that it would have been obvious to administer the 10% glycine diet of Sullivan to an obese or overweight animal. (*Id.* at 22–24.)

We conclude that the Examiner's Sullivan based rejection suffers from the same infirmity as the Kelley based rejection. That is, the Sullivan rats were young rats. (Sullivan 77.) We do not disagree with the Examiner that it was observed that the animals supplemented with 10% glycine compared to those provided an unsupplemented diet not only did not gain weight, but in fact lost six to nine grams from their original weight. (*Id.* at 78.) However, Dr. Cavagnaro explained that it is not clear whether the reduction in "carbohydrate percentage from the already very sub-optimal basal diet"[11], less food consumption (a variable that was not tracked), or glycine was the cause of the animals losing weight. (Cavagnaro Declaration ¶¶ 18–24.) We find Dr. Cavagnaro's discussion in this regard persuasive. Furthermore, the Examiner has not provided sufficient evidence to support that the Sullivan animal model would have provided one of ordinary skill in the art with any expectation in an obese or overweight animal, which animals would have a different basal nutritional/amino acid/energy requirement than the young rats of Sullivan.

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[11] The base diet was clearly suboptimal according to Dr. Cavagnaro because the rats given the unsupplemented base diet gained only 80 grams after 142 days, whereas rats fed a normal diet would have been expected to gain about 400 grams over that same time period. (Cavagnaro Declaration ¶¶ 19–20.)

In light of the foregoing, we reverse the Examiner's rejection of:

(i) Claims 1–4, 8–10, 19, 22, 26, 27, and 29–31 under 35 U.S.C. § 103(a) as unpatentable over Sullivan, McCarty, Kalman, and Yuan,

(ii) Claims 11, 20, and 21 under 35 U.S.C. § 103(a) as unpatentable over Sullivan, McCarty, Kalman, Yuan, and McLean; and

(iii) Claims 19, 24, 25, and 28 under 35 U.S.C. § 103(a) as unpatentable over Sullivan, McCarty, Kalman, Yuan, and Swenseid.

C. The Abe based rejections

The Examiner finds that Abe discloses "a mixture containing a mixture of amino acids including glycine that has a body temperature raising effect, thereby stimulating the metabolism to improve the basal metabolism and reduce body fat accumulation." (Non-Final Action 27.) The Examiner points to two examples in which glycine was part of the composition and present in a mole percent of 19.5 and 19.1, where the composition increased body temperature. (*Id.* at 27–28 (citing Abe ¶ 28, Tables 2 and 3, Figures 1 and 2, and Example 2).) The Examiner acknowledges that Abe does not teach administration of this mixture of amino acids to an overweight or obese animal. (*Id.* at 28.)

The Examiner relies on McCarty, Kalman, and Yuan as described above in the Kelley based rejection to conclude that it would have been obvious to administer a diet that contained glycine within the 10 to 30% range claimed to an obese or overweight animal. (*Id.* at 28–30.)

We again disagree with the Examiner's conclusion of obviousness. Here again, we find the Examiner's position lacking in evidence. That is the Examiner has not provided any evidence to establish the model of Abe in

which 8 to 10 week old rats that were not obese or overweight would have been used by one of ordinary skill in the art to make predictions about results that could reasonably be expected in an overweight or obese animal that has a different basal nutritional/amino acid/energy requirement, and none of the additional prior art relied upon by the Examiner plugs this hole.

Thus, we reverse the Examiner's rejection of:

(i) Claims 1–4, 8–10, 22, 24–27, and 29–31 under 35 U.S.C. § 103(a) as unpatentable over Abe, McCarty, Kalman, and Yuan

(ii) Claims 11, 20, and 21 under 35 U.S.C. § 103(a) as unpatentable over Abe, McCarty, Kalman, Yuan, and McLean; and

(iii) Claims 24, 25, 28, and 29 under 35 U.S.C. § 103(a) as unpatentable over Abe, McCarty, Kalman, Yuan, and Swenseid.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
26, 27	112, 1st	Written Description	26, 27	
30	112, 1st	Written Description		30
1–4, 8–11, 19–22, 24–31	112, 2nd			1–4, 8–11, 19–22, 24–31
20, 21	112, 2nd		20, 21	
2, 4, 10	112, 4th		2, 4, 10	
1–4, 8–10, 19–22, 24–31	103	Kelley, McCarty, Kalman, Yuan		1–4, 8–10, 19–22, 24–31

11, 20, 21	103	Kelley, McCarty, Kalman, Yuan, McLean		11, 20, 21
24, 25, 28, 29	103	Kelley, McCarty, Kalman, Yuan, Swenseid		24, 25, 28, 29
1–4, 8–10, 19, 22, 26, 27, 29–31	103	Sullivan, McCarty, Kalman, Yuan		1–4, 8–10, 19, 22, 26, 27, 29–31
11, 20, 21	103	Sullivan, McCarty, Kalman, Yuan, McLean		11, 20, 21
19, 24, 25, 28	103	Sullivan, McCarty, Kalman, Yuan, Swenseid		19, 24, 25, 28
1–4, 8–10, 22, 24–27, 29–31	103	Abe, McCarty, Kalman, Yuan		1–4, 8–10, 22, 24–27, 29–31
11, 20, 21	103	Abe, McCarty, Kalman, Yuan, McLean		11, 20, 21
24, 25, 28, 29	103	Abe, McCarty, Kalman, Yuan, Swenseid		24, 25, 28, 29
Overall Outcome			2, 4, 10, 20, 21, 26, 27	1, 3, 8, 9, 11, 19, 22, 24, 25, 28–31

AFFIRMED-IN-PART