



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/182,354	07/30/2008	Herbert T. Nagasawa	135714.00211	3624
80512	7590	01/30/2013	EXAMINER	
Pepper Hamilton LLP 400 Berwyn Park 899 Cassatt Road Berwyn, PA 19312-1183			PESELEV, ELLI	
			ART UNIT	PAPER NUMBER
			1623	
			MAIL DATE	DELIVERY MODE
			01/30/2013	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE PATENT TRIAL AND APPEAL BOARD

---

*Ex parte* HERBERT T. NAGASAWA

---

Appeal 2012-000864  
Application 12/182,354  
Technology Center 1600

---

Before TONI R. SCHEINER, LORA M. GREEN, and  
ERICA A. FRANKLIN, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a method of increasing ATP and glutathione in a mammal in need thereof and a method of treating hypoxia in a mammal in need thereof by increasing glutathione and ATP. The Patent Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm-in-part.

STATEMENT OF THE CASE

The invention concerns administering RibCys (Ribose-Cysteine) to a mammal to increase both ATP and glutathione (GSH). (Spec. 4-5.) The Specification states:

As well as functioning as a prodrug for cysteine, administration of effective amounts of RibCys can deliver amounts of ribose to ATP-depleted tissues that stimulate the *in vivo* synthesis of ATP and that also can stimulate the synthesis of NADPH (nicotinamide adenine dinucleotide phosphate, reduced). This coenzyme supplies the electrons to glutathione reductase, which in turn recycles oxidized GSH via GSSG to free GSH, which resumes its protective role as a cofactor for antioxidant enzymes in the cell.

(*Id.* at 5, ll. 14-20.)

Claims 23-40 are on appeal. Claims 23, 27, and 30 are representative and read as follows:

23. A method of increasing ATP and glutathione in a mammal in need thereof comprising administering an effective amount of RibCys or a pharmaceutically acceptable salt thereof to said mammal, wherein said RibCys increases both ATP and glutathione.

27. The method of claim 23, wherein said RibCys is administered in a unit dosage form comprising 20% (w/w) of RibCys.

30. A method of treating hypoxia in a mammal in need thereof by increasing glutathione and ATP comprising administering an effective amount of RibCys or a pharmaceutically acceptable salt thereof to said mammal, wherein said RibCys increases glutathione and ATP to treat said hypoxia.

The Examiner rejected claims 23-40 under 35 U.S.C. § 103(a) as unpatentable over Roberts,<sup>1</sup> Ozawa,<sup>2</sup> and St. Cyr.<sup>3</sup>

### OBVIOUSNESS

The Examiner's position is that Roberts disclosed that administering RibCys increases glutathione (GSH) levels, but did not specifically teach administration of RibCys to mammals in need of both increased levels of glutathione and ATP, or for the treatment of hypoxia. (Ans. 4.)

Regarding dependent claims 25, 26, 38, and 39, which are directed to liquid administration of RibCys further comprising an effective amount of ribose to inhibit premature dissociation of the RibCys, the Examiner found that Roberts disclosed that increased levels of ribose inhibited dissociation of RibCys in liquid. (*Id.* at 4-5.) Regarding dependent claims 27 and 36, directed to a unit dosage form comprising 20% (w/w) of RibCys, the Examiner found that this concentration is within the range disclosed by Roberts. (*Id.* at 5.) Further, the Examiner found that “[i]t would have been within routine experimentation by a person of ordinary skill in the art at the time of the claimed invention to establish the optimal concentration of RibCys in liquid.” (*Id.*)

The Examiner found that Ozawa disclosed a correlation between depressed levels of glutathione and the overproduction of active oxygens in

---

<sup>1</sup> Jeanette C. Roberts and David J. Francetic, *Mechanisms of Chemoprotection by RibCys, a Thiazolidine Prodrug of L-Cysteine*, 1 MED. CHEM. RES., 213-219 (1991).

<sup>2</sup> US Patent No. 5,631,234 issued to Takayuki Ozawa et al., May 20, 1997.

<sup>3</sup> Patent No. US 6,218,366 B1 issued to John St. Cyr et al., Apr. 17, 2001.

relation to ischemia, and that these active oxygens are detected in mitochondria that produce ATP. (*Id.*)

The Examiner found that St. Cyr disclosed that one condition that produces hypoxia is acute or chronic ischemia and further disclosed a method of raising the hypoxic threshold in a mammal by administering ribose. (*Id.*)

The Examiner reasoned that

Based on the teachings [of] Roberts et al, Ozawa et al and St. Cyr et al, a person having ordinary skill in the art at the time of the claimed invention would have been motivated to administer RibCys to a mammal in need of increased levels of glutathione and ATP and to treat hypoxia in a mammal by administration of RibCys because such a person would have had a reasonable expectation of success.

(Ans. 5-6.)

Regarding claims 23-29, Appellant asserts that the Examiner has not established that “the combination of . . . references discloses administering RibCys to a mammal in need of increasing both ATP and glutathione. . . .” (App. Br. 20.) According to Appellant, a proper construction of the claims, which recite a “method of increasing ATP and glutathione in a mammal in need thereof” (*see, e.g.*, Claim 23) “is that the method be practiced in order to provide the specific outcome, which in this instance is an increase in ATP and glutathione” (App. Br. 19)(citing *Jansen v. Rexall Sundown*, 342 F.3d 1329, 1333-34 (Fed. Cir. 2003)). Appellant asserts that the claimed method must not be construed “as a statement of effect that may or may not be desired or appreciated.” (*Id.* at 20.) Additionally, Appellant asserts that the Examiner has not shown that one of skill in the art would have had a

reasonable expectation of successfully increasing ATP and glutathione by administering RibCys. (*Id.*) According to Appellant, while St. Cyr disclosed administering ribose results in an increase of ATP, ribose and Ribose-Cysteine are different molecules and the Examiner has not shown that the two are equivalents such that it would have been obvious to simply substitute one for the other. (*Id.*)

Regarding claims 30-40, Appellant asserts that the Examiner has not established that “the combination of the references discloses administering RibCys to a mammal in need of increasing both ATP and glutathione to treat hypoxia” (*id.* at 23) or that “one of skill in the art would have had a reasonable expectation of success in treating hypoxia by increasing ATP and glutathione by the administration of RibCys” (*id.* at 24).

Appellant also asserts that dependent claims 25-27, 36, 38 and 39 are also not obvious and that in the Final Rejection the Examiner did not specifically address the limitations in these claims. (*Id.* at 25.) The Examiner specifically discussed these rejections in the Answer, as set forth above. (Ans. 4-5.) In the Reply Brief, Appellant asserts that this discussion in the Answer constitutes a new ground of rejection. (Reply Br. 4.) Appellant acknowledges that the reference used in the rejection are the same as in the Final Rejection, but asserts that Appellant has “not had a ‘fair opportunity to react to the thrust of the rejection’ for all of the claims.” (*Id.*)(quoting *In re Kronig*, 539 F.2d 1300, 1302-03 (CCPA 1976)).

Also in the Reply Brief, Appellant addresses the Examiner’s rationale for rejecting these dependent claims. Appellant asserts that the Examiner has not provided evidence or even an explanation establishing that it would have been within routine experimentation by a person of ordinary skill in the

art at the time of the invention to establish the optimal concentration of RibCys in liquid. (Reply Br. 6.) Further, regarding dependent claims 27 and 36, directed to a unit dosage form comprising 20% (w/w) of RibCys, Appellant asserts that “no range is disclosed in Roberts.” (*Id.* at 7.) Rather, Appellant asserts that Roberts disclosed testing “distinct amounts of RibCys, such as 1 mg/ml, 10 mg/ml and 100 mg/ml.” (*Id.*)

Regarding dependent claims 25, 26, 38, and 39, which are directed to liquid administration of RibCys further comprising an effective amount of ribose to inhibit premature dissociation of the RibCys, Appellant acknowledges that Roberts disclosed that “the initial rapid dissociation seen in Figure 1A was also eliminated with increasing concentration of ribose.” (*Id.*)(citing Roberts 215). However, Appellant asserts that Roberts did “not teach or suggest that this would be effective in the presently claimed method or that it would only require routine experimentation to inhibit premature dissociation of RibCys in the context of the presently claimed invention.” (*Id.*)

### *Analysis*

#### *I. Independent Claim 23 and Dependent Claims 24, 28, and 29*

After considering all the evidence and arguments, we conclude that the record supports a conclusion of prima facie obviousness for independent claim 23. In particular, we are not persuaded of nonobviousness by Appellant’s assertion that the prior art did not teach or suggest administering RibCys to a mammal in need of increasing both ATP and GSH. (*See App. Br. 20.*) Roberts disclosed a method of administering RibCys to reduce hepatotoxicity by increasing GSH. (Roberts 214; Ans. 4.) Roberts explained that RibCys is a prodrug of L-cysteine. (Roberts 214.) As

described in the Background of the Invention of the instant Specification, the biosynthesis of GSH involves two sequential reactions that utilize ATP and that are catalyzed by two enzymes using three precursor amino acids L-glutamic acid, L-cysteine, and glycine. (Spec. 1, ll. 22-25.) Also as acknowledged by the Specification:

All substrate-level reactants occur at near enzyme-saturating concentrations *in vivo* with the exception of L-cysteine, whose cellular concentration is exceedingly low. Therefore, the first reaction in which L-cysteine is required, i.e., the synthesis of  $\gamma$ -L-glutamyl-L-cysteine, is the rate-limiting step of glutathione biosynthesis. Thus, the availability of intracellular L-cysteine is a critical factor in the overall biosynthesis of GSH, [and] sufficient stores of ATP.

(*Id.* at ll. 26-31.) Thus, we find that a subject in need of increased GSH, e.g., to reduce hepatotoxicity as discussed by Roberts, would have particularly been a subject in need of the factors required for the biosynthesis of GSH, i.e., L-cysteine and sufficient stores of ATP. Roberts' administration of RibCys to such patients inherently provided both of these factors, although Roberts' discussion of the compound was directed primarily to its function as a prodrug of L-cysteine. *See MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999) ("Where ... the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results."); *see also Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368, 1375-76 (Fed. Cir. 2005) and *In re Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990) (both noting that an appreciation of a new benefit of an old process does not render that process patentable).

Accordingly, we affirm the rejection of independent claim 23. Appellants have not raised separate arguments for the rejection of claims 24, 28, and 29, which depend from claim 23. Accordingly, we also affirm the rejection of these dependent claims.

II. Dependent claims 25 and 26

In the Reply Brief, Appellant asserts that the Examiner's articulation of the reasons allegedly supporting the rejection of claims 25-27, 36, 38, and 39 for the first time in the Answer constitutes a new ground of rejection that merits reopening prosecution. (Reply Br. 4-5.) When an Appellant believes that an Examiner's Answer contains a new ground of rejection not identified as such, the Appellant may file a petition to the Director under 37 C.F.R. § 1.181(a) within two months of the mailing date of the Examiner's Answer requesting that a ground of rejection set forth in the Answer be designated a new ground of rejection or the argument is waived. *See* MPEP § 1207.03(IV). There is no record of Appellant having filed such a petition in this matter. Since no new ground of rejection has been designated, prosecution may not be re-opened. *See id.*; 37 C.F.R. § 41.39.

Also in the Reply Brief, Appellant asserts that dependent claims 25 and 26 would not have been obvious to a skilled artisan at the time of the invention. Claims 25 and 26 require the administration of RibCys to further comprise an effective amount of ribose to inhibit premature dissociation of the RibCys. (App. Br. 28, Claims App'x.) As Appellant acknowledges, Roberts disclosed that increased levels of ribose inhibited dissociation of RibCys in liquid. (*See* Reply Br. 7; Ans. 4-5.) Thus, we agree with the Examiner that a person of ordinary skill in the art would have found it obvious to administer an effective amount of ribose to inhibit premature

dissociation of the liquid RibCys administered in the method of Roberts based upon this disclosure in Roberts. Appellant has not persuasively established otherwise my merely asserting that Roberts did “not teach or suggest that this would be effective in the presently claimed method or that it would only require routine experimentation to inhibit premature dissociation of RibCys in the context of the presently claimed invention.” (Reply Br. 7.)

Accordingly, we affirm the rejection of dependent claims 25 and 26.

III. Dependent claim 27

Dependent claim 27 is directed to a unit dosage form comprising 20% (w/w) of RibCys. (App. Br. 28, Claims App’x.) We agree with Appellant that Roberts’ disclosure of testing “distinct amounts of RibCys, such as 1 mg/ml, 10 mg/ml and 100 mg/ml” did not teach or suggest a range of unit dosage forms, i.e., a range between 1 and 100mg/ml, such that the claimed 20% (w/w) would have been obvious. (Reply Br. 7.) Moreover, we do not find that the Examiner established that a skilled artisan would have achieved this claimed unit dosage form with routine experimentation. (See Ans. 5.)

Accordingly, we reverse the rejection of dependent claim 27.

IV. Independent Claim 30 and Dependent Claims 31-40

After considering all the evidence and arguments, we agree with Appellant that the record does not support a conclusion of prima facie obviousness for independent claim 30, which is directed to administering RibCys to treat hypoxia. (See App. Br. 28, Claims App’x.) The Examiner found that Roberts did not disclose administering RibCys to treat hypoxia. (Ans. 4.) The Examiner found that Ozawa disclosed a correlation between depressed levels of glutathione and the overproduction of active oxygens in relation to ischemia, and that these active oxygens are detected in

mitochondria that produce ATP. (*Id.* at 5.) Additionally, the Examiner found that St. Cyr disclosed that acute or chronic ischemia produces hypoxia and further disclosed a method of raising the hypoxic threshold in a mammal by administering ribose. (*Id.*) However, what is missing from the rejection is some articulated reasoning with some rational underpinnings to support the Examiner's conclusory statement that:

Based on the teachings [of] Roberts et al, Ozawa et al and St. Cyr et al, a person having ordinary skill in the art at the time of the claimed invention would have been motivated to administer RibCys to a mammal in need of increased levels of glutathione and ATP and to treat hypoxia in a mammal by administration of RibCys because such a person would have had a reasonable expectation of success.

(Ans. 5-6.) *See In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006); *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417-18 (2007). In other words, the Examiner has not explained what would have led one of ordinary skill in the art to combine the relevant teachings of the cited prior art to arrive at the claimed invention of treating hypoxia with RibCys. *See In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988).

Accordingly, we reverse the rejection of independent claim 30 and its dependent claims 31-40.

#### SUMMARY

We affirm the rejection of claims 23-26, 28, and 29;  
we reverse the rejection of claims 27 and 30-40.

Appeal 2012-000864  
Application 12/182,354

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-IN-PART

cdc