

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

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Ex parte YUAN-TSONG CHEN

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Appeal No. 2005-0410  
Application No. 09/902,461

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HEARD: May 19, 2005

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Before ELLIS, GRIMES, and GREEN, Administrative Patent Judges.

ELLIS, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal pursuant to 35 U.S.C. § 134 of claims 1-9 and 11-23, all the claims remaining in the application. Claim 10 has been canceled.

Claims 1, 19, 21 and 22 are representative of the subject matter on appeal and read as follows:

1. A method of treating glycogen storage disease type II in a human individual having glycogen storage disease type II, comprising administering to the individual a therapeutically effective amount of human acid glucosidase periodically at an administration interval, wherein the human acid  $\alpha$ -glucosidase was produced in chinese [sic, Chinese] hamster ovary cell cultures.

19. The method of claim 1, wherein the human acid  $\alpha$ -glucosidase is administered in conjunction with an immunosuppressant.

21. A method of treating cardiomyopathy associated with glycogen storage disease type II in a human individual having glycogen storage disease type II, comprising administering to the individual a therapeutically effective amount of human acid  $\alpha$  glucosidase periodically at an administration interval, wherein the human acid  $\alpha$  glucosidase was produced in chinese [sic, Chinese] hamster ovary cell cultures.

22. A pharmaceutical composition comprising human acid  $\alpha$  glucosidase, wherein the human acid  $\alpha$  glucosidase was produced in chinese [sic, Chinese] hamster ovary cell culture, in a container, the container having a label containing instructions for administration of the composition for treatment of glycogen storage disease type II.

The references relied upon by the examiner are:

Fuller et al. (Fuller), "Isolation and characterisation of a recombinant, precursor form of lysosomal acid  $\alpha$ -glucosidase." Eur. J. Biochem., vol. 234, pp. 903-909, (1995).

Bijvoet et al. (Bijvoet), "Recombinant human acid  $\alpha$ -glucosidase: high level production in mouse milk, biochemical characteristics, correction of enzyme deficiency in GSDII KO mice." Human Molecular Genetics, vol. 7, pp. 1815-1824, (1998).

The claims stand rejected as follows:

- I. Claims 1-9 and 11-23 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the appellant regards as his invention.
- II. Claims 1-4, 9, 21 and 23 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Fuller.
- III. Claims 1-7, 11-18, 21 and 23 stand rejected under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative under 35 U.S.C. § 103(a) as obvious over, Fuller.

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IV. Claims 1-9 and 11-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bijvoet in view of Fuller.

V. Claims 1-9 and 11-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Fuller.

We have carefully considered the respective positions of both the appellant and the examiner and find ourselves in substantial agreement with that of the appellant. Accordingly, we reverse Rejections I-V.

#### Background

The specification discloses that glycogen storage disease type II (GSD-II, a.k.a. Pompe disease or acid maltase deficiency) “is a fatal genetic muscle disorder caused by a deficiency of acid  $\alpha$ -glucosidase (GAA), a glycogen degrading lysosomal enzyme.” Specification, p. 1, lines 7-9. The specification further discloses that this “deficiency results in lysosomal glycogen accumulation in almost all tissues of the body, with cardiac and skeletal muscle being the most seriously affected.” *Id.*, lines 12-14. The specification still further discloses:

Clinically, GSD-II encompasses a range of phenotypes differing as to age of onset, organs involved and clinical severity, generally correlating with the residual amount of GAA activity. In its most severe presentation (infantile GSD-II, or Pompe disease, in which less than 1% of normal GAA activity is present), infants are affected by a hypertrophic cardiomyopathy, generalized muscle weakness and hypotonia secondary to massive glycogen accumulation in cardiac and skeletal muscles . . . The disease progresses rapidly, with death from cardiac failure usually occurring by 1 year of age. Juvenile (1-10% of

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normal GAA activity) and adult-onset (10-40% of normal GAA activity) forms of the disease are characterized by lack of severe cardiac involvement, later age of onset, and slower progression, but eventual respiratory or limb muscle involvement results in significant morbidity and mortality for the affected individuals [specification, para. bridging pp. 1-2].

As indicated by the claims above, the present invention is directed to a method of treating Pompe disease using the enzyme human acid  $\alpha$ -glucosidase (which is produced in Chinese hamster ovary (CHO) cells), and a pharmaceutical composition comprising said enzyme.

### Discussion

#### I. Indefiniteness

The examiner argues that the claims are vague and indefinite in the recitation of “periodically.” Answer, p. 4. According to the examiner, it is not clear what constitutes the periodic administration of a drug. Id.

We disagree.

Claims are given their broadest reasonable interpretation consistent with the description of the invention in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989); In re Prater, 415 F.2d 1393, 1404, 162 USPQ 541, 550 (CCPA 1969). In construing the claims, we begin with the words themselves. To that end, we point out that “the words of a claim are generally given their ordinary and accustomed meaning unless it appears from the specification or file history that

they were used differently by the inventor.” Carroll Touch Inc. v. Electro Mechanical Systems, 15 F.3d 1573, 1577, 27 USPQ2d 1836, 1840 (Fed. Cir. 1993).

In reading the words in the claims, we find that one skilled in the art<sup>1</sup> would have understood the “ordinary and accustomed meaning” of “periodically” to be “at regular intervals” or “from time to time,” as set forth in the Merriam-Webster Dictionary attached as Exhibit A of the appellant’s brief. Thus, we find that said person would have understood that the claimed method is directed to the administration of human acid  $\alpha$ -glucosidase “at regular intervals” or “from time to time.”

Moreover, in turning to the specification<sup>2</sup> we find that the appellant has used the term “periodically” in a manner consistent with the dictionary definition. That is, we find that the specification discloses that the phrase “periodically at an administrative

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<sup>1</sup> We point out that our appellate reviewing court has repeatedly stated that “the best indicator of claim meaning is its usage in context as understood by one of skill in the art at the time of the invention.” Moba v. Diamond Automation, Inc., 325 F.3d 1306, 1315, 66 USPQ2d 1429, 1435 (Fed. Cir. 2003); see also, Ferguson Beauregard v. Mega Sys., LLC, 350 F.3d 1327, 1338, 69 USPQ2d 1001, 1009 (Fed. Cir. 2003)(“The words used in the claims must be considered in context and are examined through the viewing glass of a person skilled in the art”); Markman v. Westview Instruments, Inc., 52 F.3d 967, 986, 34 USPQ2d 1321, 1335 (Fed. Cir. 1995) en banc, aff’d 517 U.S. 370 (1996)(“The focus is on the objective test of what one of ordinary skill in the art at the time of the invention would have understood the term to mean”).

<sup>2</sup> “It is important here to understand that under this analysis claims which on first reading – in a vacuum, if you will – appear indefinite may upon a reading of the specification disclosure or prior art teachings become quite definite.” In re Moore, 439 F.2d 1232, 1235 n.2, 169 USPQ 236, 238 n.2 (CCPA 1971).

interval”<sup>3</sup> refers to administration intervals which will vary depending on the needs of the individual; i.e., depending on the nature and extent of the disease’s effects. Id., lines 20-26. The intervals are said to be determined by standard clinical techniques. Id., line 29.

Thus, in our view, one skilled in the art would have understood, if not from the “ordinary and accustomed meaning” of the words themselves, then certainly from the teachings of the specification, that the periodic administration of human acid  $\alpha$ -glucosidase “need not be a fixed interval, but can be varied over time, depending on the needs of the individual.” Specification, p. 10, lines 1-3. That is, such person would have understood the claimed “periodically at an administrative interval” to mean “as needed” by the patient and as determined by a professional caretaker.

## II. Anticipation

The examiner argues that Fuller discloses that a recombinant precursor form of human acid  $\alpha$ -glucosidase is administered to a patient to treat Pompe disease. Answer, p. 4. The examiner contends that

. . . since the enzyme is being administered to an individual that it is inherent to that individual that they would suffer from the types of diseases claimed in claims 2-4 since the individuals are not defined in claim 1 as suffering from those specific types of diseases. As stated in Fuller, the claimed enzyme can be

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<sup>3</sup> We point out that the contested term “periodically” does not stand alone in the claims. Rather, it is part of the phrase “periodically at an administrative interval.”

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administered to a patient since it is clear from [sic, from] their results that it would treat the claimed disease. . . [Answer, p. 4].

We point out that it is well established that anticipation requires that each and every limitation set forth in a claim be present, either expressly or inherently, in a single prior art reference. In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999); Celeritas Techs. Ltd v. Rockwell Int'l Corp., 150 F.3d 1354, 1360, 47 USPQ2d 1516, 1522 (Fed. Cir. 1998); Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co., 730 F.2d 1452, 1458, 221 USPQ 481, 485 (Fed. Cir. 1984). “Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” Id. at 1269, 20 USPQ2d at 1749 (quoting In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

There is no requirement that an anticipating reference provide specific examples of the appellant’s invention; however, it must “be enabling and describe the applicant’s invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention.” In re Paulsen, 30 F.3d 1475, 1479, 31 USPQ2d 1671, 1673

(Fed. Cir. 1994). Here, we do not find that Fuller's statement that it "believes" that human acid  $\alpha$ -glucosidase produced in CHO cells "will be a useful candidate for replacement therapy in GSD II patients," provides such disclosure. A "belief" or hope that something will work is not an affirmative (i.e., an express) teaching of the claimed method of treating a GSD-II patient by administering the enzyme "periodically at administrative intervals." Nor does a "belief" that the enzyme will be a useful candidate for replacement therapy provide an inherent disclosure of said method. We point out that no successful enzyme replacement therapies were known in the art at the time of the invention. See, the Brief, p. 7. A "belief" that a compound might be of therapeutic value is merely a statement of a possibility which would not manifestly have enabled a person skilled in the art to "make and use" the claimed invention. As discussed above, inherency cannot be established by probability or possibility. In re Oelrich, 666 F.2d at 581, 212 USPQ at 326. Moreover, we find the examiner's arguments that Fuller anticipates the claimed method to be inconsistent with his statements with respect to Rejection III. That is, we find that in Rejection III, the examiner states that Fuller does not teach the amounts of human acid  $\alpha$ -glucosidase to employ, the method of administration of the enzyme or the intervals at which the enzyme should be administered. See, the Answer, p. 5, lines 3-6. Having reached such a conclusion, it is not clear to us why the examiner did not re-evaluate his position and withdrawn the § 102 rejection.

From the foregoing it reasonably follows that we do not find that Fuller inherently discloses the treatment of the various stages of Pompe's disease as recited in claims 2-4, or the disease symptom (cardiomyopathy) recited in claim 21, using human acid  $\alpha$ -glucosidase produced in CHO cells.

Accordingly, Rejection II is reversed.

### III. Anticipation and/or Obviousness over Fuller

The examiner argues with respect to claims 1-7, 11-18, 21 and 23, that Fuller either anticipates or renders obvious the amounts of CHO cell-produced human acid  $\alpha$ -glucosidase "used" [sic, claimed?], the method of administration of said human acid  $\alpha$ -glucosidase, and the intervals at which the enzyme is administered. Answer, p. 5. The examiner acknowledges that "[i]t is not clearly apparent from the reference if these limitations are present or not, but it is inherent or in the very least obvious to use the amount, methods of administration and intervals claimed." Id.

We have addressed the issue of whether Fuller anticipates, either expressly or inherently, the claimed invention, supra. With respect to the issue of obviousness, we point out that it is well established that the examiner has the initial burden under § 103 to establish a prima facie case. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); In re Piasecki, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984). It is the examiner's responsibility to show that some objective teaching

or suggestion in the applied prior art, or knowledge generally available [in the art] would have led one of ordinary skill in the art to combine the references to arrive at the claimed invention. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996). Moreover, the applied prior art must not only contain a suggestion to arrive at the claimed invention, but it must also provide evidence indicating that it would be successful. In re Eli Lilly & Co., 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990); In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

We have carefully considered Fuller's statement that "we believe it [human acid  $\alpha$ -glucosidase] will be a useful candidate for replacement therapy in GSD II patients," but find that given the teachings of the reference, it presents the type of "obvious to try" situation our appellate reviewing court has cautioned against. In re Eli Lilly & Co., 902 F.2d at 945, 14 USPQ2d at 1743; In re O'Farrell, 853 F.2d at 903-04, 7 USPQ2d at 1681. That is, Fuller discloses the production of human acid  $\alpha$ -glucosidase in CHO cells and the importance of mannose 6-phosphate (Man6P) groups on the enzyme for efficient cellular uptake via the Man6P receptor. Fuller, p. 903, col. 2. Fuller further discloses that the recombinant enzyme is efficiently endocytosed by in vitro cultures of fibroblasts and muscle cells derived from GSD II patients. Id., p. 906, col. 2- p. 908, col. 1, line 2. However, Fuller does not disclose the administration of the recombinant enzyme to art-recognized animal models, or suggest any administration protocols for

use in humans. Thus, we find that Fuller's disclosure is a general one which "may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued." In re Eli Lilly & Co., 902 F.2d at 945, 14 USPQ2d at 1743. Since Fuller only suggests a general approach to a promising field without direction, and said suggestion would require one of ordinary skill in the art to vary all the parameters of dosage amounts, intervals, routes of administration, etc., without knowing which would be successful, we find that the reference would not have provided said person a reasonable expectation of success in using human acid  $\alpha$ -glucosidase to treat GSD-II patients. In re Eli Lilly & Co., 902 F.2d at 945, 14 USPQ2d at 1743; In re O'Farrell, 853 F.2d at 903-04, 7 USPQ2d at 1681.

Accordingly, Rejection III is reversed.

#### IV. Obviousness in view of Bijvoet and Fuller

The examiner argues that Bijvoet discloses "that recombinant human acid  $\alpha$ -glucosidase is administered to a patient to treat Pompe's disease." Answer, p. 5. The examiner acknowledges that Bijvoet does not disclose "that the enzyme is a precursor of recombinant human acid  $\alpha$ -glucosidase produced in Chinese hamster ovary cells, the amounts used, the interval used to administer the enzyme, to use an

immunosuppressant or that instructions are included with the enzyme for administration.” Id., pp. 5-6. Nevertheless, the examiner contends that

[i]t would have been obvious that the enzyme is a precursor of recombinant human acid  $\alpha$ -glucosidase and that Chinese hamster ovary cells were used to produce the claimed enzyme since Fuller teaches that the claimed enzyme can be produced in hamster ovary cells and that the enzyme is a precursor of recombinant human acid  $\alpha$ -glucosidase since such desirable results are obtained with such an enzyme. . . .

The adjustment of particular conventional working conditions (e.g., determining [the] result effective amounts of the enzyme beneficially taught by the cited references, the interval the enzymes are administered, the method of administration of the enzyme, etc., especially within the broad ranges instantly claimed) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan [Answer, p. 6].

First, we do not agree with the examiner’s initial premise that Bivjoet discloses the administration of human acid  $\alpha$ -glucosidase to a patient to treat Pompe disease. Rather, we find that Bivjoet discloses the production of the enzyme in transgenic mice and its administration to (i) cultured fibroblasts and muscle cells derived from GSD-II patients; and (ii) GSD-II knock-out mice.

Second, although there is evidence of record which indicates that the human acid  $\alpha$ -glucosidase produced in transgenic mice is not identical to the human acid  $\alpha$ -glucosidase produced in CHO cells [see, Reuser (para. bridging pp. S108-109) attached as Exhibit C to the Brief;<sup>4</sup> see also, the specification, p. 6, lines 8-13], Bivjoet does not

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<sup>4</sup> Reuser, et al. (Reuser), “Enzyme therapy for Pompe disease: from science to industrial enterprise,” Eur. J. Pediatr., vol. 161, pp. S106-S111 (2002).

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report any differences. To the contrary, Bivjoet discloses that the recombinant enzyme produced in milk (transgenic mice) and CHO cells had similar activity in both in vitro and in vivo assays. Bivjoet, p. 1819, col. 2, last sentence; p. 1822, col. 1, paras. 3-4. Thus, Bivjoet concludes that

Altogether, the production of recombinant human acid  $\alpha$ -glucosidase in the mammary gland of transgenic animals seems a good alternative to production by CHO cells because of lower intrinsic costs and similar therapeutic potential. Guided by these positive results, we have started large-scale production of recombinant acid  $\alpha$ -glucosidase in the milk of transgenic rabbits [emphasis added] [Bivjoet, p. 1822, col. 1, para.5].

We do not find that given these teachings, one of ordinary skill in the art would have been motivated to employ the human acid  $\alpha$ -glucosidase taught by Fuller (i.e., the enzyme produced in CHO cells). To the contrary, we find that Bivjoet would have, at best, suggested the use of the recombinant enzyme produced in transgenic mice to treat GSD-II patients. On this record, the only suggestion we find to pursue claimed methods of treating GSD-II patients using the enzyme produced in CHO cells and administering said enzyme “periodically at administrative intervals” is in the appellant’s disclosure. Thus, we find that the examiner has engaged in impermissible hindsight to arrive at the conclusion that the claimed invention would have been obvious over Bivjoet and Fuller. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed. Cir. 1985); W.L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313 (Fed. Cir. 1983) cert. denied 469 U.S. 851 (1984)(“To imbue one of ordinary

skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher”).

Third, although we find no motivation to combine the teachings of Fuller and Bijvoet to arrive at the claimed invention, we also point out that the assays disclosed in the applied prior art, do not appear to provide one of ordinary skill in the art a reasonable expectation of success in treating human GSD-II patients. Fuller only discloses in vitro studies with cultured fibroblasts and skeletal muscle cells taken from GSD-II patients. Although the studies look promising, no follow-up testing using art-recognized animal models is reported. Bijvoet, on the other hand, tests the recombinant enzymes produced in transgenic mice and CHO cells in what is said to be an art-recognized animal model for the severe infantile form of human GSD-II (viz., GSD-II knock-out mice). Bijvoet, p. 1819, col. 2, lines 3-8. However, Bijvoet only administers a single intravenous dosage of the enzymes to 8- and 16- week old mice. The mice were sacrificed two days later. Bijvoet reports finding increased levels of human acid  $\alpha$ -glucosidase in the liver and spleen, as well as “significant” levels in heart, skeletal muscle and other organs. Id., lines 11-15. However, Bijvoet did not continue the studies to ascertain whether the treatment had any beneficial effects on the mice. Thus, given the limited results from Bijvoet’s experiments, we cannot conclude

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from the present record that those having ordinary skill in the art would have had a reasonable expectation that the administration of human acid  $\alpha$ -glucosidase to GSD-II patients would be successful.

Accordingly, Rejection IV is reversed.

#### V. Obviousness in view of Fuller

The examiner argues that in view of the teachings of Fuller,

[i]t would have been obvious to use an immunosuppressant since such medications are commonly used to suppress the immune system to better administer drugs and the like, reducing the possibility of rejection of the drug by the immune system. To include instructions in with the enzyme is obvious since the enzyme is going to be used for the same purpose as claimed (as taught by the references [sic, reference]) thus one would want to know how to administer the enzyme [Answer, p. 7].

Given our disposition of the obviousness rejection over Fuller with respect to claims 1-4, 9, 21 and 23 above, it reasonably follows that we do not find that the reference would have suggested to one of ordinary skill in the art to include (i) an immunosuppressant, and (ii) instructions for treating GSD II patients, with the human acid  $\alpha$ -glucosidase taught therein. We remind the examiner that obviousness must be based on facts, not unsupported generalities. In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1057 (1968); In re Freed, 425 F.2d 785, 787, 165 USPQ 570, 571 (CCPA 1970).

Accordingly, Rejection V is reversed.

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New Ground of Rejection

Under the provisions of 37 C.F.R. § 41.50(b), we enter the following new ground of rejection.

Claim 22 is rejected under 35 U.S.C. § 102(b) as being anticipated by Fuller.

As indicated on page 2, above, claim 22 is directed to a pharmaceutical composition comprising human acid  $\alpha$ -glucosidase produced in CHO cells in a container with a label having instructions as to how it is to be administered to a patient having GSD II. We find no difference between the claimed composition and the human acid  $\alpha$ -glucosidase produced in CHO cells disclosed in Fuller. Neither placing of the composition in a container, nor adding instructions for administration to the label, impart any new properties on the composition. One cannot obtain a patent for a known product simply by changing the label on the container in which it is placed. In re Ngai, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004) (“If we were to adopt Ngai’s position, anyone could continue patenting a product indefinitely provided they add a new instruction sheet to the product”). Accordingly, we find that the composition taught by Fuller anticipates the pharmaceutical composition set forth in claim 22.

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz.

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Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

(1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .

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(2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

REVERSED, NEW GROUND OF REJECTION

JOAN ELLIS	)	
Administrative Patent Judge	)	
	)	
	)	
	)	
	)	BOARD OF PATENT
ERIC GRIMES	)	APPEALS
Administrative Patent Judge	)	AND
	)	INTERFERENCES
	)	
	)	
	)	
LORA M. GREEN	)	
Administrative Patent Judge	)	

JE/eld

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