

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 36

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte RICHARD D. DIMARCHI,
ROGER G. HARRISON, and RONALD K. WOLFF

Appeal No. 2004-0250
Application No. 09/226,412

ON BRIEF¹

Before WINTERS and WILLIAM F. SMITH, Administrative Patent Judges, and
McKELVEY, Senior Administrative Patent Judge.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 30 through 67. Subsequently, claims 33 and 47 were canceled, leaving claims 30 through 32, 34 through 46, and 48 through 67 for our consideration on appeal.

¹ Appellants requested an oral hearing in conjunction with this appeal (Paper No. 33, June 20, 2003). However, for reasons developed infra, the merits panel has decided that an oral hearing at this time would not be an appropriate use of appellants' and the agency's resources. Accordingly, we decide this appeal on brief. 37 CFR § 1.194(c) ("If the Board decides that a hearing is not necessary, the Board will so notify appellant."). This opinion also contains new grounds of rejection under 37 CFR § 1.196(b). If appellants elect to proceed under 37 CFR § 1.196(b)(2), they may request that an oral hearing be held in conjunction with the request for rehearing.

Claims 30, 50, and 59 are representative of the subject matter on appeal and read as follows:

30. A method of administering a monomeric insulin analog comprising, administering an effective amount of the monomeric insulin analog to a patient in need thereof by pulmonary means, wherein said monomeric insulin analog:

a) is selected from the group consisting of modified human insulins wherein:

i) the amino acid residue at position B28 is substituted with Lys, Leu, Val, Asp, or Ala, and the amino acid residue at position B29 is Lys or Pro;

ii) the amino acid residues at positions B28, B29, and B30 are deleted; or

iii) the amino acid residue at position B27 is deleted; and

b) is inhaled through the mouth of said patient.

50. A method for treating diabetes comprising, administering an effective dose of monomeric insulin analog to a patient in need thereof by pulmonary means.

59. A method for treating hyperglycemia comprising, administering an effective does of a monomeric insulin analog to a patient in need thereof by pulmonary means.

The reference relied upon by the examiner is:

Jensen et al. (Jensen)	5,898,028	Apr. 27, 1999 ²
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² Jensen was filed on March 20, 1998, and is stated to be related to Provisional Application No. 60/041648 filed on March 27, 1997. In addition, the face of the Jensen Patent indicates that a claim for priority under 35 U.S.C. § 119 is made on the basis of Denmark 0319/97 filed on March 20, 1997.

Patent documents discussed by this merits panel are:

Rubsamen	5,364,838	Nov. 15, 1994
Baker et al. (Baker)	5,504,188	Apr. 2, 1996
Chance et al. (Chance)	5,514,646	May 7, 1996
Gonda et al. (Gonda)	5,743,250	April 28, 1998

Claims 30 through 32, 34 through 46, 48 through 67 stand rejected under 35 U.S.C. § 102(e) as anticipated by Jensen. In reviewing the examiner's rejection, we find ourselves in agreement with the examiner's conclusion that Jensen is an anticipation under 35 U.S.C. § 102(e) and that the proffered declarations under 37 CFR § 1.131 are ineffective in removing Jensen as a basis for rejection. However, we reach our conclusion based upon a significantly different basis than the examiner. Thus, we denominate our affirmance of this rejection as a new ground of rejection under 37 CFR § 1.196(b). In addition, we make additional rejections under 37 CFR § 1.196(b) on other prior art grounds.

Background

The claimed invention is directed to administering a monomeric insulin analog to a patient in need. Claim 30 is specific to the modified human insulins to be administered and requires that the stated modified human insulins be "inhaled through the mouth of said patient" by "pulmonary means." Claims 50 and 59 on the other hand do not require the specific monomeric insulin analogs of claim 30 and only require that the monomeric insulin analog be administered by "pulmonary means."

Insulin is used to treat patients suffering from diabetes mellitus. Specification, page 1. A certain percentage of diabetics self-administer one or more doses of insulin per day by subcutaneous injection. Id., page 2. A non-injectable form of insulin is

desirable to increase patient compliance and to avoid the discomfort associated with subcutaneous injections. Id., pages 1 and 3. Appellants report that insulin administration by way of an inhalation aerosol has been known since 1925. Id., page 3. As observed, the claimed invention is not directed to the administration of human insulin, but monomeric insulin analogs. As explained:

Insulin is a peptide hormone with a molecular weight of approximately 5,800 Daltons. In the presence of zinc, human insulin self-associates into a stable hexamer form. The dissociation of the stable hexamer is believed to be the rate limiting step in the absorption of insulin from the subcutaneous injection site to the blood stream. Rapid-acting insulin analogs, however, do not readily form stable hexamers. These analogs are known as monomeric insulin analogs because they are less prone to self-associate to stable higher-ordered complexes. This lack of self-association is due to modifications in the amino acid sequence of human insulin that decrease association by disrupting the formation of dimers. Unfortunately, the modifications to insulin which cause these analogs to be monomeric, also result in non-specific aggregation of monomers. This non-specific aggregation can render the analogs insoluble and unstable.

Specification, paragraph bridging pages 5 and 6. A preferred monomeric insulin analog used in the present invention is Asp^{B28} and an “even more preferred” monomeric insulin analog used in the present invention is Lys^{B28}Pro^{B29} (Lyspro). Id., page 8.

The working examples of the present specification report the results of experiments involving pulmonary administration of Lyspro to beagle dogs. Dogs were chosen since “they are large animals with respiratory tract deposition of particles similar to man.” Id., page 23.

Discussion

Jensen has been applied under 35 U.S.C. § 102(e). The Jensen patent is based on an application filed on January 6, 1999, and claims benefit of Provisional Application No. 60/070752 filed January 8, 1998. Appellants have not contested that the claims of Jensen are entitled to the earlier filing date of March 27, 1997 of Provisional Application No. 60/041648. Indeed, their argument on appeal, *i.e.*, the declarations filed under 37 CFR § 1.131³ are effective to remove the rejection premised upon Jensen, allege a conception date prior to March 27, 1997. *See, e.g.*, Declaration II, para. 3.⁴ The examiner has concluded:

The Jensen '028 reference is a U.S. patent or U.S. patent application publication of a pending or patented application that claims the rejected invention. An affidavit or declaration is inappropriate under 37 CFR § 1.131(a) when the reference is claiming the same patentable invention, see MPEP § 2306. If the reference and this application are not commonly owned, the reference can only be overcome by establishing priority of invention through interference proceedings. See MPEP Chapter 2300 for information on initiating interference proceedings.

Examiner's Answer, paragraph bridging pages 4 and 5.

In response, appellants argue that an interference cannot be declared between the present application and Jensen since no interference-in-fact exists between

³ There are three declarations under 37 CFR § 1.131 of record. The first was received August 17, 2000 (Paper No. 11) (Declaration I), the second received January 18, 2002 (Paper No. 21) (Declaration II), and the third received June 20, 2002 (Paper No. 24) (Declaration III).

⁴ We note that the "Protocol Summary for Study Design Approval Committee" attached to Declaration II includes the heading "Study Design Approval Date: March 18, 1997," which date is prior to the March 20, 1997 date of the Jensen priority claim under 35 U.S.C. § 119.

appellants' claims and Jensen's claims. Reply Brief, page 2. Appellants explain that this Board requires a two-way test be applied to determine whether claims in a patent application and an issued patent are directed to the same patentable invention, citing Winter v. Fujita, 53 USPQ2d 1234, 1243 (Bd. Pat. App. & Int. 1999). Appellants then explain why the two-way test does not apply under the present circumstances.

Appellants are correct that the so-called two-way test must be met before an interference can be declared. Eli Lilly & Co. v. Board of Regents of the Univ. of Wash., 334 F.3d 1264, 1270, 67 USPQ2d 1161, 1166 (Fed. Cir. 2003) (“[W]e hold that the Director’s interpretation of 37 CFR § 1.601(n) as establishing a two-way test for determining whether two parties are claiming the ‘same patentable invention’ is neither plainly erroneous nor inconsistent with the language of the regulation.”).⁵ We have considered appellants’ position set forth in the Reply Brief as to why the two-way test cannot be met under the present circumstances, i.e., the Jensen patent claims are patentably distinct from the claims pending in this application. We disagree and find that the two-way test is met.

The relevant Jensen patent claims are claims 1, 14, and 15, which read as follows:

1. A therapeutic powder formulation suitable for pulmonary administration, comprising particles which comprise (i) human insulin, any analogue or derivative thereof, or combinations of the foregoing; and (ii) an enhancer which enhances the absorption of insulin in the lower respiratory tract, wherein at least 50% by weight of said particles are crystalline and herein the molar ratio of insulin to enhancer is between about 9:1 and 1:9.

⁵ The present real party in interest is Eli Lilly and Company. Amended Brief, page 2.

14. A method of treating diabetes, comprising administering to a subject in need thereof a therapeutically effective amount of the powder formulation according to claim 1.

15. A method of treating diabetes according to claim 14, wherein said insulin analogue is Lys^{B28}Pro^{B29} human insulin or Asp^{B28} human insulin.

Appellants argue that method claims 14 and 15 of Jensen are patentably distinct from the method claims of the present application because:

In contrast to the claims in the Jensen '028 patent, the claims in the present application do not recite three of the four limitations required by the Jensen '028 claims. Specifically, the claims in the present application do not recite

- (1) an enhancer,
- (2) the percent weight crystalline parameter, or
- (3) the molar ratio parameter required by the claims of the Jensen '028 patent.

Thus, the claims in the present application do not anticipate the claims in the Jensen '028 patent.

Further, the claims in the present application do not render obvious the claims in the Jensen '028 patent. Nowhere in the claims in the present application is there a suggestion of (1) an enhancer, (2) a percent weight crystalline requirement, or (3) a molar ratio parameter of insulin analog to enhancer. In addition, one of ordinary skill in the art would not be motivated by the claims of the present invention to use an enhancer, or to use 50% by weight of crystalline particles, or to use a particular ratio of insulin analog to enhancer.

Reply Brief, page 5.

Appellants are correct in stating that the claims in the present application do not recite an enhancer, the percent weight crystalline parameter or the molar ratio parameter set forth in claims 14 and 15 of Jensen. However, appellants' analysis does not view the present claims in light of relevant prior art in determining whether the present claims render the Jensen claims obvious under 35 U.S.C. § 103. The relevant

prior art under the two-way test is (1) the claimed subject matter of this application (which is assumed to be prior art) in combination with (2) other relevant prior art.

Turning to the first difference noted by appellants, i.e., an enhancer, we note that independent claims 30, 50, and 59 of this application are “comprising” in nature and thus, are open to the inclusion of other substances. Jensen describes the enhancer in the following manner:

The expression ‘enhancer’ refers to a substance enhancing the absorption of insulin, insulin analogue, or insulin derivative through the layer of epithelial cells lining the alveoli of the lung into the adjacent pulmonary vasculature, i.e., the amount of insulin absorbed into the systemic system is higher than the amount absorbed in the absence of enhancer.

Jensen, column 2, lines 15 through 21. Jensen states that the enhancer is “advantageously a surfactant.” Id., column 2, lines 59 through 61. The present specification states that the monomeric insulin analog compositions administered according to the claimed method may also include surfactants. See, e.g., Id., page 15, line 19.

Furthermore, it is known in the art that surfactants assist in the absorption of monomeric insulin analogs including Lyspro by mucosal surfaces. Chance describes monomeric insulin analog composition including Lyspro compositions that include absorption enhancing agents such as oleic acid. See Chance, column 52, lines 35 through 50. Thus, it would have been obvious to one of ordinary skill in the art to use a surfactant in the compositions administered in present claims 30, 50, and 59 and expect that the surfactant would serve as an “enhancer,” i.e., enhancing the absorption of the monomeric insulin analog by the lung.

Turning to the second difference noted by appellants, i.e., the percent weight crystalline parameter required by the Jensen claims, we note the present specification states that monomeric insulin analogs which form part of this invention are those described in U.S. Patent 5,504,188 (Baker). See, specification, page 21, line 25. The title of Baker is "Preparation of Stable Zinc Insulin Analog Crystals." Baker describes preparation of crystalline insulin analogs including crystalline Lyspro. Thus, one of ordinary skill in the art would have found it obvious to use crystalline monomeric insulin analogs in the method set forth in claims 30, 50, and 59 of this application. The use of crystalline Lyspro as the sole monomeric insulin analog in the present invention would have been understood by one skilled in the art to result in 100% by weight of the particles being crystalline. Thus, the at least 50% by weight limitation would have been obvious.

The last difference between the respective claims appellants point to is the molar ratio parameter required by the Jensen claims. Jensen requires that the molar ratio of insulin to enhancer be between about 9:1 and 1:9. As set forth above, the present specification states that surfactants may be used in the monomeric insulin analog formulations administered by claims 30, 50, and 59. In describing that surfactants may be used, appellants did not set forth any finite amounts in which those surfactants should be present. Under these circumstances, appellants have left it to the skill of the art to determine an appropriate amount of surfactant to be used in implementing this embodiment of the present invention. It should also be kept in mind that Chance describes the use of surfactants as enhancers in formulating monomeric insulin analog

preparations. Thus, one of ordinary skill in the art would need to determine an optimum amount of surfactant to be used to perform the enhancer function described in Chance. As set forth in In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980), it is normally prima facie obvious for a person of ordinary skill in the art to optimize a result effective parameter. Thus, one of ordinary skill in the art, in implementing the surfactant embodiment described in the specification, would have found it obvious to optimize the amount of surfactant to be used to perform the enhancer function described by Chance. Appellants have not shown by way of objective evidence that such an optimized amount would not be within the ratios required by Jensen claims 14 and 15.

From the above analysis, it is seen that the subject matter of the present claims viewed in light of relevant prior art render obvious the subject matter of Jensen claims 14 and 15. Thus, this aspect of the two-way test is met. Appellants have not provided a fact-based analysis as to why the other aspect of the two-way test is not met under the present circumstances. In other words, appellants have not explained why Jensen claims 14 and 15 do not anticipate or render obvious the claims pending in this application. Thus, the two-way test is met and the examiner was correct in not accepting appellants' showings under 37 CFR § 1.131. Since we have explained for the first time in this case why the two-way test has been met, we denominate our

affirmance of the examiner's rejection as a new ground of rejection under 37 CFR § 1.196(b).⁶

The question now becomes one of priority of invention. However, for the reasons set forth below, the claims pending in this application are unpatentable on grounds apart from those based upon Jensen. Thus, declaration of an interference is premature. However, if claims are determined to be patentable in subsequent proceedings but for Jensen, we make the following observations in regard to the three declarations filed under 37 CFR § 1.131.

If the question of interference subsequently arises, based upon the respective filing dates, appellants must make a showing under 37 CFR § 1.608(b). As set forth in the rule, that evidence shall include if possible, "one or more corroborating witnesses, supported by documentary evidence." The three Rule 131 declarations of record do not address the issue of corroboration.

Furthermore, appellants assert in Declaration II that "conception of an invention encompassing the pulmonary delivery of Lys^{B28}Pro^{B29}-human insulin occurred prior to March 27, 1997 and was diligently reduced to practice on April 18, 1997." It would be

⁶ Appellants argued the claims on appeal as a group with the exception of claims 49, 53, and 62 directed to the use of AspB28-human insulin. It is believed that appellants separately argued the merits of those three claims in light of Declaration III directed to establishing AspB28 and Lyspro possess similar biochemical and biophysical properties. Since Jensen describes the use of both AspB28-human insulin and Lyspro, we have addressed the merits of all claims subject to the examiner's rejection that have been separately addressed in the briefing and see no reason to extend the analysis of the patentability issues in regard to Jensen further than appellants and the examiner have done, especially since we set forth detailed reasons why all of the pending claims are unpatentable in the other new grounds of rejection that follow.

helpful in any Rule 608(b) showing if appellants provide evidence in support of the assertion that they were diligent in their pursuit of a reduction to practice. Given the relatively short time period between March 27, 1997 and April 18, 1997, a day-by-day accounting of the alleged diligent activity would be helpful.

New Grounds of Rejection Based Upon Gonda '250

Claims 30, 31, 32, 34-46, and 48 are rejected under 35 U.S.C. § 102(e) as anticipated by Gonda '250.

Turning first to claim 30, we find that claim 30 is directed to a method of administering a monomeric insulin analog to a patient in need thereof by “pulmonary means.” The monomeric insulin analog required by claim 30 is selected from a Markush group which includes modified human insulins wherein the amino acid residue at position B28 is substituted with Lys and the amino acid residue at position B29 is Pro, i.e., Lyspro. The other requirement of claim 30 is that the monomeric insulin analog be inhaled through the mouth of the patient.

Considering first the requirement of claim 30 that the monomeric insulin analog be administered to the patient by “pulmonary means,” we note in Unidynamics v. Automatic Prod. Int'l, 157 F.3d 1311, 1319, 48 USPQ2d 1099, 1104 (Fed. Cir. 1998) (citation omitted) the court stated that “[t]he use of the term ‘means’ generally (but not always) shows that the patent applicant has chosen the option of means-plus-function format invoking § 112, ¶ 6 construction.” As set forth in 35 U.S.C. § 112, sixth paragraph, if a claim limitation invokes this section of the statute, it must be interpreted to cover the corresponding structure, materials, or acts in the specification and

“equivalents thereof.” Neither appellants nor the examiner have favored the record with their position as to whether the claim limitation “pulmonary means” invokes the sixth paragraph of § 112, and, if so, what corresponding structure is described in the present specification. However, Gonda ‘250 describes a device that provides an aerosolized insulin formation to be delivered to a patient’s lungs by way of inhalation through the mouth of the patient. See, e.g., the abstract of Gonda ‘250 and Figure 3. For the purposes of this appeal, we will consider that the Gonda ‘250 device is a “pulmonary means” as this term is used in the claims on appeal.⁷

Thus, the question becomes whether Gonda ‘250 describes the administration of a modified human insulin analog such as Lyspro in that manner. Gonda ‘250 states that the methods described in that patent may be used to administer insulin analogs, specifically stating: “Other general types of insulin analogs are presently used. One type of new analog is sold by Lilly [the present real party in interest] under the name Lyspro and this analog is absorbed faster after subcutaneous injection.” Gonda ‘250, column 28, lines 53 through 56. See also, Gonda ‘250, column 29, lines 34 through 35 (“Other than Lyspro, the insulin analogs are not presently used for the treatment of patients on a commercial scale.”).

From the above analysis, it is seen that Gonda ‘250 describes the method required by claim 30 on appeal and thus constitutes an anticipation. The earliest date of invention alleged by appellants in the Rule131 declarations of record is March 27,

⁷ In the event of further prosecution, appellants and the examiner should address this issue and resolve whether “pulmonary means” does invoke the requirements of 35 U.S.C. § 112, sixth paragraph.

1997. Since the application from which Gonda '250 issued was filed on November 22, 1996, it is apparent that the Rule 131 declarations are ineffective.

Claims 31, 32, 34-46, and 48 which depend from claim 30 are also described in Gonda '250 as discussed in the following table:

Table 1

<p>Claims 31-32 directed to delivering the monomeric insulin analog to a lower airway of the patient, specifically the alveoli.</p>	<p>Gonda '250, column 3, lines 59-60 (“[I]t is desirable to get the aerosolized insulin formulation deeply into the lung.”) In view of this disclosure it is reasonable to shift the burden to appellants to establish through objective evidence that the method described in Gonda '250 does not deliver the insulin to the lower airway of the patient, e.g., the alveoli. <u>In re Best</u>, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).</p>
<p>Claims 34-36 directed to administering the monomeric insulin analog by way of an aerosol with the analog being in a pharmaceutical carrier such as an aqueous medium.</p>	<p>Gonda '250, column 4, lines 6-10, (“systemic delivery of insulin is obtained by releasing an aerosolized dose at a prescribed point in a patient’s respiratory cycle.”) Gonda '250, column 40, lines 52-56 (“[T]he insulin may be an aqueous solution of the drug....”)</p>
<p>Claims 37-40 directed to administering the monomeric insulin analog as a dry powder having specified particle sizes, e.g., less than 10 microns.</p>	<p>Gonda '250, column 40, lines 58-64 (The drug may be in powder form having particle size in the range of 0.5-12 microns.)</p>
<p>Claim 41 directed to at least 10% of the monomeric insulin analog delivered is deposited in the lung.</p>	<p>See the analysis set forth above in regard to claims 31-32. It is again reasonable to shift the burden to appellants to provide objective evidence that the method of Gonda '250 does not meet this claim limitation.</p>

Claims 42-44 directed to use of an inhalation device such as a nebulizer, meter-dosed inhaler, dry powder inhaler or sprayer.	See the analysis set forth above in regard to claims 37-40.
Claims 45-46 directed to using a dry powder inhaler to administer specified dosages of the monomeric insulin analog.	Gonda '250 describes a wide range of dosages. See, e.g., column 31, lines 33-45. It is reasonable to shift the burden to appellants to establish by way of objective evidence that the dosages required by claims 45-46 differ from those described in Gonda '250. <u>In re Best, supra.</u>
Claim 48 directed to Lyspro	Gonda '250 describes the use of Lyspro in that method.

Claim 49 is rejected under 35 U.S.C. § 103(a). As evidence of obviousness we rely upon Gonda '250.

Claim 49 is directed to the use of AspB28 human insulin in the claimed method. As set forth in Declaration III, it was "well known" at the time of filing this application that AspB28 human insulin and Lyspro had "similar biochemical and biophysical properties." Dec. III, paragraph 2. Thus, it would have been obvious to one of ordinary skill in the art at the time of the present invention to use AspB28 human insulin as the monomeric insulin analog of Gonda '250.

Independent claims 50 and 59 are rejected under 35 U.S.C. § 102(e) as anticipated by Gonda '250.

Claims 50 and 59 respectively require administration of an effective dose of monomeric insulin analog for the purpose of treating diabetes or hyperglycemia to a

patient in need thereof by pulmonary means. These claims place no limitation on the monomeric insulin analog to be administered.

As developed above in regard to claim 30, Gonda '250 describes the administration of monomeric insulin analogs to patients in need thereof by way of "pulmonary means." One purpose of the invention of Gonda '250 is to control the symptoms of diabetes, i.e, control the blood glucose level of diabetic patients. See, e.g., Gonda '250, column 13, line 39-column 14, line 7. Thus, Gonda '250 describes the treatment of diabetic patients who are hypoglycemic and hyperglycemic.

Dependent claims 51-58 and 60-67 are rejected under 35 U.S.C. § 102(e) as anticipated by Gonda '250.

These dependent claims contain the same limitations as the dependent claims discussed in Table 1 above and, thus, are unpatentable for the corresponding reasons.

Rejections Based upon Rubsamen

Independent claims 50 and 59 are rejected under 35 U.S.C. § 102(b) as anticipated by Rubsamen.

Claims 50 and 59 respectively require administration of an effective dose of monomeric insulin analog for the purpose of treating diabetes or hyperglycemia to a patient in need thereof by pulmonary means. These claims place no limitation on the monomeric insulin analog to be administered.

Rubsamen describes the administration of monomeric insulin analogs to patients in need thereof by way of "pulmonary means." Id., column 5, lines 28-40 (analog) and

column 2, line 65-column 3, line 38 (pulmonary means). One purpose of the invention of Rubsamen is to control the symptoms of diabetes, i.e, control the blood glucose level of diabetic patients. See, e.g., id., column 8, line 18-57. Thus, Rubsamen describes the treatment of diabetic patients who are hypoglycemic and hyperglycemic in the manner required by claims 50 and 59.

Dependent claims 51, 54-57, 60 and 63-66 are rejected under 35 U.S.C. § 102(b) as anticipated by Rubsamen.

Rubsamen is applied as above. The details of these dependent claims are accounted for as follows:

Table 2

Claims 51 and 60 directed to administering the monomeric insulin analog as a pharmaceutical formulation using a pharmaceutically acceptable carrier.	Rubsamen, column 14, lines 40-45
Claims 54-55, 63-64 directed to delivering the monomeric insulin analog by way of an inhalation device such as a sprayer or dry powder inhaler in the lungs of the patient.	Rubsamen, column 14, lines 40-60
Claims 56-57 and 65-66 directed to specific amounts of the monomeric insulin analog to be administered.	Rubsamen, column 5, lines 55-68 In view of this disclosure it is reasonable to shift the burden to appellants to establish through objective evidence that the amounts of the insulin analog delivered in Rubsamen do not meet those required by these claims. <u>In re Best</u> , 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).

Independent claim 30 and dependent claims 41, 48, 52, 58, 61, and 67 are rejected under 35 U.S.C. § 103(a). As evidence of obviousness we rely upon Rubsamen and Chance.

These claims differ from the method described in Rubsamen by requiring a specified monomeric insulin analog such as Lyspro. Chance describes Lyspro and the advantages it possesses over native human insulin. *Id.*, Column 1, lines 14-20 (“[Lyspro] is less prone to dimerization or self-association to higher molecular weight forms thereby possessing a comparatively more rapid onset of activity while retaining the biological activity of native human insulin.”).

It would have been obvious to one of ordinary skill in the art to use Lyspro as the monomeric insulin analog in Rubsamen for the advantages described by Chance. As to the requirement of claim 41 that at least about 10% of the monomeric insulin be delivered to the lung, we direct attention to column 9, lines 23-35 of Rubsamen.

Dependent claims 31, 32, 34-40, and 42-46 are rejected under 35 U.S.C. § 103(a). As evidence of obviousness, we rely upon Rubsamen and Chance.

The references are combined for the reasons set forth above. The limitations added by these dependent claims are accounted for as follows:

Table 3

<p>Claims 31 and 32 directed to delivering the monomeric insulin analog to a lower airway of the patient, e.g., the alveoli.</p>	<p>The method of Rubsamen provides for delivery of the active agent to the lungs of the patient. <u>Id.</u>, column 17, lines 6-10. In view of this disclosure it is reasonable to shift the burden to appellants to establish through objective evidence that the method described in Rubsamen does not deliver the insulin to the lower airway of the patient, e.g., the alveoli. <u>In re Best</u>, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).</p>
<p>Claims 34-37 and 42-44 directed to formulating the monomeric insulin analog with a pharmaceutical carrier, including suspending the active agent in a non-aqueous medium, administering the active agent in the form of an aerosol and/or a dry powder, using an inhalation device such as a metered dose inhaler or a dry powder inhaler.</p>	<p>Rubsamen describes administering a monomeric insulin analog in the form of an aerosol containing the active agent in the form of a powder with or without a non-aqueous propellant using an inhalation device. See column 14, line 40-column 15, line 30 and column 20, line 62-column 21, line 9.</p>
<p>Claims 38-40 directed the particle size of the monomeric insulin analog.</p>	<p>The monomeric insulin analog of Rubsamen is used in the form of a powder. As such, it would have been obvious to optimize the particle size of the powder as this is a result effective variable. <u>In re Boesch</u>, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980).</p>
<p>Claims 45-46 directed the amount of monomeric insulin analog to be administered.</p>	<p>Rubsamen, column 5, lines 55-68 In view of this disclosure it is reasonable to shift the burden to appellants to establish through objective evidence that the amounts of the insulin analog delivered in Rubsamen do not meet those required by these claims. <u>In re Best</u>, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).</p>

Claims 49, 53, and 62 are rejected under 35 U.S.C. § 103(a). As evidence of obviousness, we rely upon Rubsamen and Chance.

Claims 49, 53, and 62 are directed to the use of AspB28 human insulin in the claimed method. As set forth in Declaration III, it was “well known” at the time of filing this application that AspB28 human insulin and Lyspro had “similar biochemical and biophysical properties.” Dec. III, paragraph 2. Thus, it would have been obvious to one of ordinary skill in the art at the time of the present invention to use AspB28 human insulin as the monomeric insulin analog of Rubsamen.

Other Issue

We direct attention to that part of Chance that describes intranasal administration of Lyspro. See, e.g., column 52, line 35-column 53, line 62. Lyspro was administered to the nasal cavity of dogs by way of a nebulizer. The issue this disclosure creates is whether the intranasal administration of Lyspro in Chase is an equivalent to the pulmonary means required by the claims on appeal under 35 U.S.C. § 112, sixth paragraph. Chase reports data obtained from those experiments and compares the data with that obtained by administering Lyspro subcutaneously and intravenously. It may be that a comparison of that data with the data set forth in the present specification obtained by administering Lyspro by way of pulmonary means will lead to the conclusion that administering Lyspro to the nasal cavity using a nebulizer and through “pulmonary means” are equivalents.

Time Period for Response

This opinion contains new grounds of rejection pursuant to 37 CFR § 1.196(b). 37 CFR § 1.196(b) provides that, "[a] new ground of rejection shall not be considered final for purposes of judicial review."

37 CFR § 1.196(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 proceedings (§ 1.197(c)) as to the rejected claims:

(1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner. . . .

(2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record. . . .⁸

The examiner's decision is affirmed.

⁸ Again, if appellants elect to proceed under this provision of the rule, they may request an oral hearing be scheduled.

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

AFFIRMED - 37 CFR § 1.196(b)

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Sherman D. Winters)	
Administrative Patent Judge)	
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William F. Smith)	
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Fred E. McKelvey, Senior)	
Administrative Patent Judge)	

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