

The opinion in support of the decision being entered today
is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte MARC S. GORDON, THOMAS TARARA, and
JEFFRY WEERS

Appeal 2007-2516
Application 10/302,553
Technology Center 1600

Decided: July 24, 2007

Before TONI R. SCHEINER, DONALD E. ADAMS, and RICHARD M.
LEBOVITZ, *Administrative Patent Judges*.

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DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 1-20.
We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF CASE

Lung surfactants are used to treat infant respiratory distress syndrome (Specification 1: 20-24), adult respiratory distress syndrome, and other diseases associated with decreased natural lung surfactant (Specification 2: 32 to 3: 9). According to the Specification, current methods of delivering

surfactants to the lung are inefficient (Specification 1-3). The instant application describes methods of administering lung surfactants by inhalation using dry powder compositions (Specification 3: 20-25).

Claims 1-23 are pending and rejected (Amended Br. 4). The Examiner relies on the following prior art as evidence of unpatentability:

Clements	US 5,110,806	May 5, 1992
Alliance	WO 99/16410	Apr. 8, 1999
Hafner '970	US 6,436,970 B1	Aug. 20, 2002
Hafner '223	US 6,858,223 B2	Feb. 22, 2005

The following rejections are on review in this appeal:

1) Claims 1-23 stand rejected under 35 U.S.C § 112, second paragraph as indefinite (Answer 3).

2) Claims 1-23 stand rejected under 35 U.S.C § 103(a) as obvious over Hafner '970 or Hafner '223 in combination with Alliance (Answer 4).

3) Claims 1-23 stand rejected under 35 U.S.C § 103(a) as obvious over Alliance, alone, or in combination with Clements (Answer 7).

For each prior art rejection, Appellants separately argue the following groups of claims: claims 1-15, 16-18, and 19-20. Within each grouping, the claims stand or fall together. We select claims 1, 16, and 19 as representative. They read as follows:

1. A method for providing lung surfactant therapy to a patient in need thereof, the method comprising:
decreasing an oxygen index of a patient by at least 20% by administering a dry powder composition by inhalation to the respiratory tract of a patient, the dry powder composition comprising lung surfactant and particles, the particles comprising phospholipid, and the particles having a gel to liquid crystal phase transition temperature greater than about

40°C, a bulk density of less than about 0.5 g/cm³, and a mass median aerodynamic diameter from about 0.5 - 10 µm.

16. A method for providing lung surfactant therapy to a patient in need thereof, the method comprising:

decreasing an oxygen index of a patient by at least 20% by administering a dry powder composition by inhalation to the respiratory tract of the patient, the dry powder composition comprising lung surfactant and particles, the particles comprising phospholipid and calcium, and the particles having a gel to liquid crystal phase transition temperature greater than about 40°C, a bulk density of less than about 0.5 g/cm³, and a mass median aerodynamic diameter from about 0.5 - 10 µm.

19. A method for providing lung surfactant therapy to a patient in need thereof, the method comprising:

decreasing an oxygen index of a patient by at least 40% by administering a dry powder composition as a dry powder aerosol by inhalation to the respiratory tract of a patient in a plurality of inhalations over a 30 minute period, the dry powder composition comprising lung surfactant and particles, the particles comprising phospholipid and calcium, the particles having a gel to liquid crystal phase transition temperature greater than about 40°C, a bulk density of less than about 0.5 g/cm³, and a mass median aerodynamic diameter from about 0.5 - 10 µm.

FINDINGS OF FACT

Hafner '970

1. Hafner '970 teaches that adult respiratory distress syndrome (ARDS) can be treated with lung surfactant (Hafner '970, col. 1, ll. 20-24; col. 2, ll. 9-10).
2. Lung surfactant "has surface-active properties and reduces the surface tension in the alveolar region of the lungs" (Hafner '970, col. 3, ll. 10-12).

3. “[L]ung surfactant compositions comprise phospholipids and . . . can additionally contain lung surfactant proteins” (Hafner ‘970, col. 3, ll. 42-44).
4. The lung surfactant compositions can also contain calcium to set a favorable viscosity (Hafner ‘970, col. 3, ll. 46-48).
5. Commercially available lung surfactants include “Curosurf® . . . , a highly purified natural surfactant from homogenized pigs’ lungs, Survanta® . . . and Alveofact® . . . , both extracts of bovine lungs, and also Exosurf® . . . , a synthetic phospholipid with auxiliaries” (Hafner ‘970, col. 3, ll. 48-55).
6. Hafner ‘970 describes therapeutic compositions which comprise dipalmitoylphosphatidylcholine, which is a phospholipid (Hafner ‘970, cols. 4-5, Examples 1-4), or lung surfactant purified from bovine lungs (Hafner ‘970, col. 5, ll. 40-45, Example 5).
7. The composition can be a powder (Hafner ‘970, col. 5, ll. 4-6) which is administered by inhalation (Hafner ‘970, col. 4, ll. 25-29).
8. Using an animal model for ARDS, Hafner ‘970 shows that administration of lung surfactant as powder improves lung function, leading to a desired rise in the PaO₂ (Hafner ‘970, col. 6, ll. 53-55; cols. 7-8, Tables 1 and 2; Answer 5-6).
9. Hafner ‘970 also shows that increasing surfactant dosage results in a rise in PaO₂. *See* Hafner ‘970, Tables 1 and 2, showing the effect of lung surfactant dosages of 25 mg/kg and 100 mg/kg.

Alliance

10. It is stated in the instant Specification that “[p]articularly preferred embodiments of the invention incorporate spray dried, hollow and porous particulate compositions as disclosed in WO 99/16419 [Alliance]” (Specification 7: 17-18).

11. Alliance teaches “porous perforated particles for the delivery of bioactive agents to the respiratory tract of a patient” (Answer 4). See Alliance, p. 1.
12. The particles can comprise one or more surfactants (Alliance, p. 10, ll. 18-19), including lipids (such as phospholipids (Alliance, pp. 10, ll. 26 to 11, l. 1).
13. Surfactants “may further increase dispersion stability, powder flowability, simplify formulation procedures or increase efficiency of delivery” (Alliance, p. 10, ll. 20-22).
14. “Generally compatible lipids [surfactants] comprise those that have a gel to liquid crystal phase transition greater than about 40°C” (Alliance, p. 11, ll. 3-4).
15. Exemplary phospholipids include dipalmitoylphosphatidylcholine and distearylphosphatidylcholine (Alliance, p. 11, l. 6).
16. Alliance’s compositions “typically yield powders with bulk densities less than 0.5 gm/cm³” (Alliance, p. 9, ll. 24-25).
17. Alliance teaches that “the mean aerodynamic diameter of the perforated microstructures is preferably less than about 5 μm” (Alliance, p. 29, ll. 3-4).
18. The particles can be administered as an aerosol (Alliance, p. 14, ll. 10-11).

Clements

19. Clements describes administration of lung surfactant compositions to treat respiratory distress syndrome (Clements, cols. 1-2: Answer 8).
20. A natural and synthetic lung surfactant was administered to fetal rabbits to determine the effect on lung function (Clements, cols. 8-10 (“Example III)).

DISCUSSION

Rejection under § 112, second paragraph

Claims 1-20 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite (Answer 3).

Claim 1 recites a “dry powder composition comprising lung surfactant and particles, the particles comprising phospholipid.” The Examiner contends that “[i]t is unclear whether the compositions have both lung surfactant and phospholipid or just phospholipid, which is lung surfactant” (Answer 3).

We reverse the rejection. The claim language is not unclear. In plain language, the claim recites that it comprises 1) lung surfactant and 2) particles comprising phospholipid. We see no reason to read out the lung surfactant limitation from the claim simply because phospholipid can also be characterized as a surfactant.

Consistent with the plain meaning of the claim, the Specification describes compositions which comprise a lung surfactant (“Infasurf®” at Specification 10: 5 (Example I)) and a phospholipid (DPPC or dipalmitoylphosphatidylcholine at Specification 10: 8-17 (Example I)). The Specification also states that “[t]he lung surfactant compositions suitable for use in the present invention additionally include any of those phospholipids known in the art” (Specification 5: 22-28), indicating that a lung surfactant and phospholipid were expressly contemplated by the inventors.

Rejection under § 103 over Hafner '223 or Hafner '970 combined with Alliance

Claims 1-23 stand rejected under 35 U.S.C. § 103(a) as obvious over Hafner '223 or Hafner '970 in combination with Alliance (Answer 4). Because the Examiner relies on Hafner '223 and '970 for the same teachings, we only refer to the disclosure in Hafner '970.

The Examiner states that Hafner '970 teaches administering a lung surfactant powder to treat ARDS, but does not disclose that the powder has particles possessing the properties which are recited in the claims (Answer 4). However, the Examiner asserts that Alliance teaches surfactant containing particles for aerosol administration to the lungs having the same characteristics which are claimed (Answer 4-5). The Examiner concludes that “[t]o prepare the particles of Hafner having the claimed bulk density and mass median diameter values would have been obvious to one of ordinary skill in the art since [Alliance] teaches the advantages of particles having these properties while administering compositions to the respiratory tract of a patient” (Answer 5).

We agree with the Examiner that the combination of Hafner '970 with Alliance is sufficient to establish prima facie obviousness of the claimed subject matter, shifting the burden to Appellants to provide rebuttal evidence or arguments.

Appellants admit in their Specification that the “[p]articularly preferred embodiments of the invention incorporate spray dried, hollow and porous particulate compositions as disclosed in WO 99/16419 [Alliance]” (Specification 7: 17-18; Findings of Fact 10). Consistent with this admission, the Examiner found that all the recited properties of the claimed

particles are described in Alliance, including a teaching of “a bulk density of less than about 0.5 gm/cm³” (Alliance, p. 9, ll. 24-25; Findings of Fact 15; Answer 5) and “a mass mean aerodynamic diameter from about 0.5-10 μm” (Alliance, p. 29, ll. 3-5; Finding of Facts 16; Answer 5). We find the Examiner’s conclusion reasonable that it would have been obvious to those of ordinary skill to have administered surfactant as particles for the advantages described by Alliance (Answer 4-5). Appellants do not identify a flaw in this reasoning.

Appellants argue that Alliance does not “teach that particles should have a gel to liquid crystal phase transition temperature greater than about 40°C as claimed in claim 1” (Amended Br. 13). We disagree. Alliance describes using surfactants having “a gel to liquid crystal phase transition greater than about 40°C” (Alliance, p. 11, ll. 3-4; Findings of Fact 14). Consequently, it is reasonable to presume that particles comprising the surfactant would also have a phase transition temperature greater than about 40°C.

“decreasing an oxygen index of a patient by at least 20%”

The method of claim 1 comprises a step of “decreasing an oxygen index of a patient by at least 20%.” The Examiner contends that Hafner describes compositions which contain dipalmitoylphosphatidylcholine (Hafner ‘970, cols. 4-5, Examples 1-5; Findings of Fact 6; Answer 5) for treating ARDS and therefore “one of ordinary skill in the art would [have] expect[ed] [a] similar decrease in [the] oxygen index” (Answer 5). The Examiner also asserts that

although Hafner does not specifically state decrease of oxygen index by at least 20 %, on col. 6, lines 23-40 Hafner (970)

indicates that the arterial oxygen partial pressure (PaO₂) [of] rats having respiratory distress syndrome (animal models) which was 500-550 mm hg decrease to values of 50-110 mm Hg whereas animals in control group which are not treated with lung surfactant remain with their PaO₂ at these low values. From these teachings of Hafner, one of ordinary skill in the art would expect instantly claimed oxygen index percentages.

(Answer 5-6).

Appellants challenge the Examiner's conclusion, asserting that the step of "decreasing an oxygen index of a patient by at least 20%" as recited in claim 1 would not have been obvious to one of ordinary skill in the art (Amended Br. 13).

We agree with the Examiner. Hafner expressly teaches that inhaled surfactants advantageously increase PaO₂ in an animal model for ARDS in a dose-related manner (Hafner '970, col. 6, ll. 53-55; cols. 7-8, Tables 1 and 2; Findings of Fact 8-9; Answer 6). PaO₂ is inversely proportional to the oxygen index.¹ An increase in PaO₂ would therefore lead to a decrease in the oxygen index. Thus, it would have been expected from Hafner's teaching that surfactant administration would decrease the oxygen index, the same result recited in claim 1. The difference between Hafner and claim 1 is that the claim requires that the oxygen index be decreased by a specific amount: by at least 20%. In our opinion, it would have been obvious to persons of ordinary skill in the art at the time the invention was made to have optimized administration of a surfactant composition to achieve an effective decrease in oxygen index (or rise in PaO₂ levels) for treating

¹ Oxygen index = %O₂ x MAP (mean airway pressure)/PaO₂ (partial pressure of oxygen in arterial blood (torr or mmHg)). Specification 5: 10-16.

ARDS. The discovery of an optimum value of a results-effective variable in a known process is normally obvious. *In re Antonie*, 559 F.2d 618, 620, 195 USPQ 6, 8 (CCPA 1977); *In re Aller*, 42 CCPA 824, 220 F.2d 454, 105 USPQ 233 (1955).

Appellants contend that “[u]sing the claimed particles to decrease an oxygen index of a patient by at least 20%, is both new and unexpected” (Amended Br. 13). “[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.” *In re Baxter Travenol Labs.*, 952 F.2d 388, 392, 21 USPQ2d 1281, 1285 (Fed. Cir. 1991). Appellants have not presented any comparative evidence to establish that the claimed invention in comparison to the prior art achieved unexpected results.

For the foregoing reasons, we affirm the rejection of claim 1. Claims 2-14 fall with claim 1 because they were not separately argued.

Claims 16-18

Claim 16 differs from claim 1 in reciting that the recited particles comprise calcium. Hafner ‘970 teaches that its lung surfactant can also contain calcium to set a favorable viscosity (Hafner ‘970, col. 3, ll. 45-47; Findings of Fact 4; Answer 4). We agree with the Examiner that it would have been obvious to include calcium with the surfactant for the reasons taught by Hafner ‘970. Appellants do not identify a flaw in the Examiner’s reasoning and we find none. We affirm the rejection of claim 16. Claims 17 and 18 fall with claim 16 because they were not separately argued.

Claims 19-20

Claim 19 differs from claim 1 in reciting that the oxygen index of a patient is decreased by “at least 40%” by inhaling the claimed composition “in a plurality of inhalations over a 30 minute period.” The claim also recites that particles comprise calcium.

For the reasons discussed above for the limitation in claim 1 of “decreasing an oxygen index of a patient by at least 20%,” we conclude that it would have been obvious to have optimized the administration conditions to achieve the recited degree of oxygen index reduction. We have considered Appellants’ arguments (Amended Br. 15-16), but they are no different than the arguments provided in support of the patentability of claim 1. We do not find these arguments any more persuasive for claim 19. We affirm the rejection of claim 19. Claim 20 falls with claim 19 because it was not separately argued.

Rejection under § 103 over Alliance by itself or in combination with Clements

Claims 1-23 stand rejected under 35 U.S.C. § 103(a) as obvious over Alliance by itself, or in combination with Clements (Answer).

The Examiner contends that “[a]lthough [Alliance] does not provide specific examples of powders containing DPPC and lung surfactant, from the guidance provided by [Alliance], it would have been obvious to one ordinary skill in the art to use lung surfactant and DPPC powders with claimed properties with a reasonable expectation of success, if the patient requires a lung surfactant therapy” (Answer 8). The Examiner also argues that “[s]ince WO teaches a composition which is a combination of lung

surfactant and a phospholipid which can be dipalmitoyl phosphatidylcholine and similar to instant composition, one of ordinary skill in the art would expect similar properties of the compositions” (Answer 8-9).

We reverse this rejection. Unlike the rejection over Alliance and Hafner ‘970, the Examiner does not provide sufficient evidence to show that treating with a surfactant would decrease the oxygen index and thus that Alliance or Alliance in combination with Clements would achieve a dry powder able to decrease the oxygen index by at least 20%. The rejection of claims 1-23 over Alliance or Alliance in combination with Clements is reversed.

OTHER ISSUES

In its “Definitions” section, the Specification states that lung surfactant “as used herein refers to Infasurf® . . . containing compositions which comprise an extract of natural surfactant from calf lungs” (Specification 4: 29-30). When a specification reveals a special definition given to a claim term, the inventor’s lexicography governs. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316, 75 USPQ2d 1321, 1329 (Fed. Cir. 2005) (en banc). On the record before us, there is no evidence that the Examiner considered the inventors to be their own lexicographer by interpreting the claimed “lung surfactant to mean “Infasurf® . . . containing compositions which comprise an extract of natural surfactant from calf lungs.” If further prosecution is undertaken in this case, we suggest that the Examiner consider the Specification definition of lung surfactant in interpreting the phrase “lung surfactant” as recited in the claims.

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TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv) (2006).

AFFIRMED

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