

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 ALAIN MARTIN

Appeal 2007-3747
Application 10/205,354
Technology Center 1600

Decided: October 23, 2007

Before TONI R. SCHEINER, NANCY J. LINCK, and RICHARD M.
LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 1-9 and
12-27. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Airway diseases, such as asthma, chronic obstructive pulmonary
disease (COPD), emphysema, and chronic bronchitis affect millions of
people in the United States (Specification 1-2). They account for millions of
doctor visits and claim the lives of many Americans (Specification 1-2).
Bronchial constriction and spasm are symptoms of these diseases

(Specification 5). The Specification describes the use of alpha-keto acids having four or more carbon atoms, and precursors of them, for treating bronchial constriction and spasm associated with airway diseases (Specification 4).

Appellant appeals from the Examiner's final rejection of claims 1-9 and 12-27, which are all the pending claims. The following rejections are appealed:

Claims 26 and 27 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement (Answer 4);

Claims 1, 9, 26, and 27 stand rejected under 35 U.S.C. § 102(e) as anticipated by Fink (WO 02/07430 A1, published 26 Sep. 2002) (Answer 4); and

Claims 2-8 and 12-25 stand rejected under 35 U.S.C. § 103(a) as obvious over Fink in view of Radhakrishnan (U.S. Pat. No. 5,192,528, issued Mar. 9, 1993) (Answer 4).

Within each rejection, the claims stand or fall together because separate reasons for the patentability of any individual claim were not presented. *See* 37 C.F.R. 41.37(c)(1)(vii). We focus on claims 1, 2, 12, 26, and 27 which read as follows:

1. A method for treating bronchial constriction in mammals comprising
contacting mammalian lung with an alpha-keto acid selected from the group consisting of oxaloacetic acid, ketoglutaric acid, ketobutyric acid, ketoadipic acid, ketocaproic acid, ketoisovaleric acid, their salts and mixtures thereof and precursors of these alpha-keto acids; wherein the compound is present in a therapeutically effective amount to produce bronchial dilation.
2. The method of claim 1 wherein the compound is inhaled.

12. The method of claim 1 further comprising contacting the mammalian lung with a therapeutic agent.

26. A method for treating airway disease in mammals comprising
contacting mammalian lung with an alpha-keto acid selected from the group consisting of oxaloacetic acid, ketoglutaric acid, ketobutyric acid, ketoadipic acid, ketocaproic acid, ketoisovaleric acid, their salts and mixtures thereof and precursors of these alpha-keto acids; wherein the compound is present in a therapeutically effective amount to prevent bronchial spasm.

27. A method for treating airway disease in mammals comprising
contacting mammalian lung with an alpha-keto acid selected from the group consisting of oxaloacetic acid, ketoglutaric acid, ketobutyric acid, ketoadipic acid, ketocaproic acid, ketoisovaleric acid, their salts and mixtures thereof and precursors of these alpha-keto acids; wherein the compound is present in a therapeutically effective amount to prevent bronchial constriction.

DISCUSSION

REJECTION UNDER 112, FIRST PARAGRAPH

Claims 26 and 27 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement.

“To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)).

“When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement. . . . *Marzocchi*, 439 F.2d at 223-24, 169 USPQ at 369-70.” *In re Wright*, 999 F.2d at 1561-62, 27 USPQ2d at 1513.

The Examiner contends that “the specification, while being enabling for ‘treating bronchial constriction’ or ‘treating bronchial spasms’, does not reasonably provide enablement for ‘treating airway disease’” (Answer 4).

The Examiner argues:

It is beyond the skill of pharmacologists today to get an agent to be effective against all types of airway diseases or any diseases related to airway diseases. Although the airway diseases are often characterized by bronchial constriction and/or bronchial spasms, the cause of many airway diseases is not fully known or understood (The Merck Manual, Fifteenth Edition, 1987, pp. 623-708). And the pathophysiology of the airway diseases involves multitude of factors, and it is not known yet that a single underlying mechanism ties together all of the seemingly unrelated more than 40 known airway diseases . . . Therefore, the skill[ed] artisan would turn to undue amount of trial and error to find out which airway disease would be responsive to the claimed composition.

(Answer 7-8.)

We do not find that the Examiner has sustained the burden of setting forth adequate reason to doubt the assertions made in the Specification as to the scope of enablement of claims 26 and 27. *See In re Wright*, 999 F.2d at 1562, 27 USPQ2d at 1513.

According to the Specification, alpha-keto acids having four or more carbon atoms act as bronchial dilators in mammals (Specification 5). The Specification explains:

Without being held to a specific theory of operation, it is believed that the extra cellular bronchial dilators act as a reactive oxygen species antagonist reducing the active oxygen species present in the lung. . . . When the active oxygen agents are removed, the lungs return to normal. . . . Additionally, the alpha-keto acids may act to enhance the lung's ability to remove mucus thereby clearing the lungs allowing less obstructed airflow. The alpha-keto-acids of the present may reduce the viscosity of mucus by removing hydrogen peroxide, which is known to thicken mucus. . . . The removal of mucus may also reduce the triggers present in the lung thereby reducing and/or preventing bronchial constriction and bronchial spasm.

(Specification 5-6.)

The Specification identifies typical airway diseases that cause bronchial spasm and constriction and states that the alpha-keto acids can prevent bronchial spasm and construction in such diseases (Specification 7-8). An example is disclosed in which asthma is treated with alpha-keto acids (Specification 8-9). From the data in the example, it is concluded that each of "the keto acids tested was as effective a bronchial dilator as albuterol" (Specification 9).

In sum, the Specification provides a logical explanation as to why the claimed alpha-keto acids are effective to prevent bronchial spasm and constriction in airway diseases in which these symptoms occur. A specific example is also provided in the Specification to support the assertion that therapeutic efficacy of the claimed alpha-keto acids.

The only evidence provided by the Examiner to support the position that the Specification does not provide adequate enablement for claims 26 and 27 is that bronchial spasm or constriction occurs in more than 40 “seemingly unrelated airway diseases” whose causes are “not fully known or understood” (Answer 7).

Claims 26 and 27 are directed to “treating airway disease” by administering an alpha-keto acid which is “present in a therapeutically effective amount to prevent” bronchial spasm (claim 26) or bronchial constriction (claim 27). Thus, we interpret “treating” to mean that the bronchial spasm or constriction is prevented by administration of the claimed compound. The Specification describes a mechanism for how the alpha-keto acids are believed to work in the lung (Specification 5-6; *see supra* at p. 5), providing logical underpinnings for the assertion that the compounds would be effective in airway diseases which involve bronchial spasm or constriction. While the Examiner may be correct that airway diseases differ in their pathophysiology, we do not see how this would affect the ability of the claimed alpha-keto acids to treat the underlying symptom of bronchial spasm and constriction. The Examiner has offered no evidence that the mechanism of bronchial spasm and constriction would differ in different airway diseases to the extent that their efficacy in treating asthma (Specification 9) would not reasonably predict success in other airway diseases. Thus, we conclude that the Examiner has not sustained the burden in setting forth adequate reason to doubt the assertions made in the Specification as to the scope of enablement of claims 26 and 27. See *In re Wright*, 999 F.2d at 1562, 27 USPQ2d at 1513. We reverse the enablement rejection of claims 26 and 27.

REJECTION UNDER § 102

Claims 1, 9, 26, and 27 stand rejected under 35 U.S.C. § 102(e) as anticipated by Fink.

Findings of Fact

Fink

1. Fink teaches administering alpha-ketoalkanoic acids, and their physiologically acceptable salts, to treat inflammatory conditions, including asthma (Fink, at p. 5, ll. 3-13, p. 7, l. 4, and p. 14, l. 21; Answer 10).
2. Bronchial constriction and spasm is a symptom of asthma (Specification 5).
3. Fink lists examples of useful alpha-ketoalkanoic acids, including C₃-C₈ straight-chained or branched acids, such as alpha-ketobutyrate (Fink, at p. 5, ll. 14-20; Answer 10).
4. Fink teaches that therapeutic amounts of the alpha-ketoalkanoic acids can be administered intranasally (Fink, at p. 13, ll. 15-17; Answer 10).
5. “It is known in the art that administration of drug ‘intranally’, especially anti-inflammatory steroid (i.e., mometasone, fluticasone) that is useful for the treatment asthma, would have been expected (anticipated) to reach the relevant tissue in the lung and exert the therapeutic effects of the drug (see US 5,837,699 and US 6,750,210)” (Answer 19).

Application of Fink to claim 1

6. Fink’s teaching of the treatment of asthma with an alpha-ketoalkanoic acid ((Findings of Fact (“FF”) 1) satisfies the limitation of claim of “treating bronchial constriction in mammals” since bronchial constriction is a

symptom of asthma (FF 2) and thus treating asthma would include treatment of its symptoms.

7. Fink's teaching of intranasal administration of therapeutic amounts of alpha-ketoalkanoic compounds (FF 1, 4, and 5) meets the limitations of claim 1 of "contacting mammalian lung with an alpha-keto acid."

8. Fink also teaches that the alpha-keto acid can be alpha-ketobutyrate (FF 3), which is one of the specifically listed compounds in claim 1.

9. Thus, Fink describes all the limitations of claim 1 and thus anticipates it.

Analysis

"It is well settled that a claim is anticipated if each and every limitation is found either expressly or inherently in a single prior art reference." *Celeritas Techs. Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522 (Fed. Cir. 1998). We agree with the Examiner's findings (FF 1-5) and conclude that Fink describes all elements recited in claim 1 (FF 6-9), anticipating it.

Appellant contends that Fink discusses "only the use of ethyl pyruvate" (Appeal Br. 12¹). We do not find this argument persuasive. Fink expressly discloses that alpha-ketobutyrate – a compound which falls within the scope of claim 1 – can be utilized in its treatment methods (FF 3; Fink, at p. 5, ll. 14-20; Answer 10). While ethyl pyruvate is exemplified by Fink in its example section (Specification 20), these examples do not negate Fink's explicit disclosure that alpha-ketobutyrate is also a useful compound. "All the disclosures in a reference must be evaluated, . . . and a reference is not

¹ "Appeal Br." is a reference to the Appellant's Revised Appeal Brief, dated Jul. 25, 2006.

limited to the disclosure of specific working examples.” *In re Mills*, 470 F.2d 649, 651, 176 USPQ 196, 198 (CCPA 1972).

Appellant also argues that Fink “does not teach administering the compositions into the lung by inhalation” (Appeal Br. 12, 13-14).

We are not persuaded by this argument because claim 1 does not require that the claimed keto-acid compound be administered by inhalation. Rather, claim 1 is directed to “contacting mammalian lung” with an alpha-keto acid compound. Claim 2 further limits claim 1 by reciting that “the compound is inhaled.” Thus, it is reasonable to interpret claim 1 as not being limited to “inhalation” because such interpretation would render claim 2 superfluous. Our interpretation is consistent with the Specification which describes “contacting the lungs” with an alpha-keto acid compound in its “Summary of the Invention,” and lists inhalation as a preferred embodiment along with other modes of administration (Specification 6).

Finally, Appellant contends that the “one class of compounds which are administered through one route (oral, intravenous, or topical forms) to treat one disease cannot necessarily be administered through another route (inhalation) to treat another disease (Appeal Br. 14). This argument is without merit because, as found by the Examiner (Answer 19), Fink teaches intranasal administration that meets the limitation of claim 1 of “contacting mammalian lung” (FF 5). Appellant failed to challenge the Examiner’s finding.

For the foregoing reasons, we affirm the rejection of claims 1, 9, 26, and 27 as anticipated by Fink.

REJECTION UNDER § 103

Claims 2-8 and 12-25 stand rejected under 35 U.S.C. § 103(a) as obvious over Fink in view of Radhakrishnan.

Findings of Fact

10. Radhakrishnan describes administering a corticosteroid by inhalation to treat asthma (Radhakrishnan, at col. 1, ll. 38-43; col. 3, ll. 4-6 and 15-23; Answer 11).

11. The “determination of [an] appropriate administration regimen having optimum therapeutic index [for the claimed drugs] is well considered within the level of ordinary skill in the artisan” (Answer 12-13).

12. Radhakrishnan teaches that “[i]nhalation provides an effective means for treating a variety of lung diseases . . . such as bronchial asthma An important advantage of inhalation in treating lung diseases is the ability to deliver the drug directly to the site of drug action” (Radhakrishnan, at col. 1, ll. 38-43).

Analysis

In making an obviousness determination over a combination of prior art references, it is important to identify a reason why persons of ordinary skill in the art would have attempted to make the claimed subject matter. See *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007). In this case, the Examiner provides evidence that both the claimed alpha-keto acid (FF 1; Answer 10) and corticosteroid (FF 10; Answer 11) – a therapeutic agent that meets the limitations of claim 12 – were known in the prior art for the treatment of asthma. The Examiner reasons that it would have been obvious to persons of ordinary skill in the art

to combine two therapeutic agents which were known to be useful to treat asthma (Answer 12) to achieve the subject matter of claim 12.

We agree with the Examiner's reasoning. As held by the Supreme Court, the "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR*, 127 S. Ct. at 1739, 82 USPQ2d at 1395. In this case, claim 12 is directed to a combination of two known drugs, both of which perform according to their expected properties. Since Appellant has not shown that the results of the combination are anything more than predictable, we conclude that the Examiner has sustained the burden of establishing prima facie obviousness.

Appellant contends that there is no motivation to have combined the references. They state that it "is not appropriate to combine the inhalable corticosteroid of Radhakrishnan . . . with the orally ingestible ethyl pyruvate of Fink" (Appeal Br. 19).

We do find Appellant's characterization of the rejection accurate. The Examiner has not relied upon Fink for teaching orally ingestible ethyl pyruvate. Fink is cited by the Examiner for its teaching of intranasally administrable alpha-ketobutyrate (FF 3-5; Answer 10, 19). Since both alpha-ketobutyrate and corticosteroids are known to be effective in treating asthma (FF 1, 10), we find the skilled artisan would have been motivated to utilize them in the same method of treating asthma with a reasonable likelihood of success.

In regard to claim 2, which recites that the alpha-keto acid is inhaled,² the Examiner finds that the “determination of [an] appropriate administration regimen having optimum therapeutic index [for the claimed drugs] is well considered within the level of ordinary skill in the artisan” (FF 11; Answer 12-13). Thus, in view of Radhakrishnan’s teaching that “[i]nhalation provides an effective means for treating a variety of lung diseases . . . such as bronchial asthma” (FF 12), a skilled person would have known to administer the claimed compound by inhalation, a route considered to be effective and advantageous for treating asthma (FF 12).

For the foregoing reasons, we affirm the rejection of claims 2 and 12; claims 3-8 and 13-25 fall with claims 2 and 12 because separate reasons for their patentability were not provided.

CONCLUSION

The rejection of claims 26 and 27 under § 112, first paragraph, for lack of enablement is reversed because the Examiner did not sustain the burden of providing a reasonable explanation as to why the scope of protection provided by the claims is not adequately enabled by the description of the invention. The rejections under § 102 and § 103 of claims 1-9 and 11-27 are affirmed. The Examiner established prima facie anticipation and obviousness, respectively, of the claimed subject matter;

² The Examiner found that a drug administered intranasally would reach the lungs (FF 5), but did not address whether intranasal administration would be considered “inhalation,” which, in our opinion, would be the case if the drug were inhaled through the nose.

Appeal 2007-3747
Application 10/205,354

Appellant did not come forward with persuasive arguments to rebut the Examiner's case.

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

lbg

RICHARD R. MUCCINO
758 SPRINGFIELD AVENUE
SUMMIT NJ 07901