

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 144

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

DEE W. BROOKS AND KAREN E. RODRIQUES
Junior Party

v.

TAKAFUMI IKEDA, AKIYOSHI KAWAI,
TAKASHI MANO, YOSHIYUKI OKUMURA
AND RODNEY W. STEVENS
Junior Party,

v.

SIMON T. HODGSON, PETER J. WATES,
DAVID E. DAVIES, STEVEN SMITH
AND DEREK A. DEMAINE
Senior Party

Patent Interference No. 103,378

CALVERT, DOWNEY, and LORIN, Administrative Patent Judges.

DOWNEY, Administrative Patent Judge.

Final Decision

This interference involves a patent to Brooks et al (Brooks), U.S. Patent No. 5,187,192, assigned to Abbott Laboratories, an application to Ikeda et al. (Ikeda), Serial No. 08/070,327, assigned to Pfizer, Inc., and an application to Hodgson et al. (Hodgson), Serial No. 08/050,437, assigned to Glaxo Wellcome Inc.

The subject matter at issue is defined by a single count, count 3,¹ which count includes, in alternative format, certain hydroxamic acid and N-hydroxyurea compounds of formula I, a pharmaceutical composition containing an effective amount of a compound of formula I in a carrier, and a method of inhibiting the biosynthesis of leukotrienes by administering to a mammal a therapeutical effective amount of a compound of formula I. Count 3 is found in the APPENDIX attached to this decision.

Brooks claims 1-11 and Hodgson claims 1-7, 11-17, and 21-34 and Ikeda claims (as amended) 1-10, 13-19, 23, 24, 27, 28 and 32 correspond to count 3.

During the preliminary motion stage, Ikeda moved, inter alia, for benefit of the November 27, 1990 filing date of their earlier filed Japanese application, JP 2-323814. The APJ granted the motion and Ikeda became senior party.

The parties exchanged proofs. Hodgson relied upon its November 23, 1990 priority date for their United Kingdom application, i.e., GB 9025514.2. Hodgson, having conceded that party Ikeda has established diligence from a date prior to November 23, 1990 to its priority date, November 27, 1990(IR18), filed a paper indicating that they would not file a brief and would not contest the award of priority as determined by the parties or the APJ in accord with the

¹ The interference was redeclared on October 27, 1994 to add party Ikeda et al and substitute count 2 for count 1, and redeclared again on July 7, 1995, pursuant to the decision on motions to substitute count 3 for count 2.

record.² (IR 15 and 16). Ikeda and Brooks could not decide priority between them and submitted to the Board a single issue for determination.³ To wit, have Brooks established an actual reduction to practice as of November 16, 1990⁴ when Rodriques made a compound within the scope of the count or at a later date when testing occurred as asserted by Ikeda.

The Brooks record consists of the affidavit testimony of Clint Dee W. Brooks, Michael Meyer, Douglas H. Steinman, Randy L. Bell, Karen E. Rodriques, Dr. Anthony Kreft, Robert L. Rosati and Elias J. Corey and the associated exhibits attached to each of these affidavits, excerpts from the involved Brooks, Hodgson, and Ikeda applications, and the involved U.S. Patent No. 5,187,192 issued to Brooks.

Brooks case for priority

Rodriques, a named inventor, testified that on November 13, 1990, she prepared a preparation of N-[3-phenylcyclobutyl]-N-hydroxyurea, which was

² The Brooks record, brief and exhibits will be referred to herein as BR, BB, and BX, respectively.

³ Party Brooks does not raise the issue of prior conception coupled with reasonable diligence to filing of its application. Therefore, this issue is deemed abandoned. Photis v. Lunkenheimer, 225 USPQ 948, 950 (Bd. Pat. Int. 1984). See also Estee Lauder Inc. v. L' Oreal, 120 F.3d 588, 592-93, 44 USPQ2d 1610, 1613 (Fed. Cir. 1997) (where our reviewing court stated that the district court could not examine, absent compelling circumstances, evidence directed to an issue not raised before the board).

⁴ Brooks' preliminary statement indicates that the earliest date relied upon for a reduction to practice is November 16, 1990. (See Paper No. 35, and Statement of Reliance, Paper No. 97). See 37 C.F.R. § 1.629(b) which states: [E]vidence which shows that an act alleged in the preliminary statement occurred prior to the date alleged in the statement shall establish only that the act occurred as early as the date alleged in the statement.

designated with Abbott A-code number⁵ A-79935. (BR-149, ¶ 13, Laboratory notebook # 39005, p.111). A-79935 was subjected to NMR testing, #164600 on November 14, 1990. (BR 440-49, BX-31). Rodriques stated that the NMR showed a 45:55 ratio of diastereomers in this preparation. (BR 149, ¶ 13, BR 181, BX15). Dr. Steinman is said to corroborate Rodriques' testimony. (BB 8). Dr. Bell testified that he supervised the testing of the cyclobutyl N-hydroxyurea and hydroxamic acid compounds described in the involved patent for their ability to inhibit in vitro leukotriene B₄ (LTB₄) biosynthesis in heparinized human blood and in vivo leukotriene biosynthesis in rats when dosed orally. (BR 121-22, ¶ 2). Bell testified that the computer printouts (BX-30) show that compound A-79935, prepared by Rodriques, had an in vitro HWBL IC₅₀ of 0.33µM and an in vivo ED₅₀ of 93 µmol/kg when tested on December 18, 1990 and February 21, 1991, respectively. (BR 122-23, ¶¶ 3-4).

As noted supra, Brooks conducted no tests before November 27, 1990 to establish a practical utility of compound A-79935. Notwithstanding this fact, Brooks urge that it is not necessary for them to test for utility to establish a reduction to practice because in their view, the utility of the compounds of the count is obvious. In support of their position of obviousness, Brooks rely upon the affidavit opinions of coinventor Brooks and Dr. Kreft (Kreft). Coinventor Brooks testified that he wrote the entry "5-LO", shorthand for "5-lipoxygenase", in his notebook because it was his belief that the cyclobutyl N-hydroxyureas he

⁵ An Abbott A-code number was given to a compound when it was determined to be analytically pure and submitted to the drug sample room. (BR 147, ¶ 5).

conceived “would be useful as inhibitors of 5-lipoxygenase based on my previous experience with the related cyclopropyl N-hydroxyureas which are useful for this purpose.” (BR 7-8, ¶ 9) Kreft opined that the structural similarity of the N-hydroxyureas and hydroxamic acid compounds of the count with N-hydroxyureas and hydroxamic acids known as of that time, as evidenced by documents, BX39-56, would establish that as of November 14, 1990, it was “reasonably certain” to one of skill in the relevant art that N-hydroxyureas and hydroxamic acids of the count (all being hydrophobic) would inhibit 5-LO. (BR 451, ¶¶ 3-4). Kreft said:

[T]he pharmacophore of the N-hydroxyureas and hydroxamic acids, i.e. the part of the molecule which is responsible for 5-LO inhibitory activity, is the N-hydroxyurea or hydroxamic acid portion of the molecule which is common to all the hydrophobic 5-LO inhibitory compounds discussed herein. (BR 453, ¶ 6)

Ikeda position

Ikeda argue that the Brooks evidence is not sufficient to establish utility of the prepared compound, A-79935. It is Ikeda’s position that testing was necessary because a practical utility for A-79935 cannot be “foretold with certainty” based on structural similarity of A-79935 and other N-hydroxyurea and hydroxamic acid compounds, known to be 5-LO’s.

Burden of Proof

Brooks, as the junior party whose application was copending with the Ikeda application, bear the burden to establish priority by a preponderance of the evidence. Bosies v. Benedict, 27 F.3d 539, 541-42, 30 USPQ2d 1862, 1864 (Fed. Cir. 1994).

Reduction to Practice

Reduction to practice is a question of law, which is based on underlying factual determinations. Estee Lauder, 129 F.3d at 592, 44 USPQ2d at 1613. Proof of an actual reduction to practice of a compound requires a showing of three elements: (i) production of a composition of matter satisfying the limitations of the count, (ii) recognition of the composition of matter, and (iii) recognition of a specific practical utility for the composition. Id. It is well settled that a practical utility must be established for a novel compound before it can be said to have been reduced to practice. Kawai v. Metlesics, 480 F.2d 880, 886, 178 USPQ 158, 163 (CCPA 1973). Whether a composition of matter must be tested in order to establish a reduction to practice, and if so, what tests are necessary, is a question which must be decided on the basis of the facts of the particular case involved. Blicke v. Treves, 241 F.2d 718, 720-21, 112 USPQ 472, 475 (Fed. Cir. 1957). If no utility is specified in the count, evidence establishing a substantial utility for any purpose is sufficient to prove reduction to practice. Fujikawa v. Wattanasin, 93 F.2d 1559, 1563-64, 39 USPQ2d 1895, 1898-99 (Fed. Cir. 1996) ; Rey-Bellet v. Engelhardt, 493 F.2d 1380, 1383, 181 USPQ 453, 454 (CCPA 1974).

In the pharmaceutical arts, our reviewing court has long held that practical utility may be shown by adequate evidence of any pharmacological activity. In Fujikawa, 93 F.2d at 1564, 39 USPQ2d at 1899, it said:

It may be difficult to predict, however, whether a novel compound will exhibit pharmacological activity, even when the behavior of analogous compounds is known to those skilled in the art. Consequently, testing is often required to establish practical utility. See e.g., Blicke, 241 F.2d at

720, 112 USPQ at 475.

It is also recognized that utility can be established by other than by actual testing if sufficient properties of that compound are determined such that the sought-for-utility is readily apparent, as by demonstrating a similarity of properties of the new compound to established properties of a known class of compounds having a known utility. Ciric v. Flanigen, 511 F.2d 1182, 1185, 185 USPQ 103, 105 (CCPA 1975); Anderson v. Natta, 480 F.2d 1392, 1395-96, 178 USPQ 458, 460 (CCPA 1971); Richardson v. Cook, 442 F.2d 1398, 1400-01, 170 USPQ 86, 88 (CCPA 1971); Fang v. Hankins, 399 F.2d 262, 269, 158 USPQ 345, 351 (CCPA 1968); Bindra v. Kelly, 206 USPQ 571, 575 (Bd. Pat. Int. 1979).

Opinion

We hold that party Brooks has not proved an actual reduction to practice of the subject matter of count 3 because Brooks failed to establish a practical utility for A-79935 prior to November 27, 1990.

Here the count is trifurcated and the compound portion of the count does not recite a specific utility. Brooks rely upon the utility disclosed in their application. According to the Brooks disclosure, the compounds of the count inhibit lipoxigenase enzymes, and in particular, 5-lipoxygenase (5-LO). These enzymes are the first step in the pathway leading to the production of leukotriene products. Leukotriene products are potent substances with diverse actions which produce a wide variety of biological effects, often in an extremely small concentration range. Alterations in leukotriene metabolism have been

demonstrated in a number of disease states including “asthma, allergic rhinitis, rheumatoid arthritis and gout, . . . and central nervous system pathology resulting from the formation of leukotrienes following stroke or subarachnoid hemorrhage”. (see particularly, column 1, lines 50-58 for a complete listing of all the disease states). Thus, inhibition of the 5-LO enzyme provides an approach to limit the effects of all the products of this pathway and the compounds which so inhibit 5-LO are said to be useful in the treatment of disease states in which leukotrienes play an important role. (See column 1, lines 17-20 and 50-66 of the involved Brooks patent).

To prove a reduction to practice, Brooks must show that “the embodiment relied upon as evidence of priority actually worked for its intended purpose.” Newkirk v. Lulejian, 825 F.2d 1581, 1582, 3 USPQ2d 1793, 1794 (Fed. Cir. 1987). Thus, while Brooks urges that it is obvious that compounds of the count would be 5-LO inhibitors, our focus is specific to whether Brooks established that 5-LO inhibitor activity of A-79935 could be foretold with certainty without testing.

In our view, the situation here, like that in Fisher v. Bouzard, 3 USPQ2d 1677, 1681 (Bd. Pat. App. & Int. 1987); DeSolms v. Schoenwald, 15 USPQ2d 1507, 1510-11 (Bd. Pat. App. & Int. 1990) and Bigham v. Godtfredsen, 222 USPQ 632, 636 (Bd. Pat. Int. 1984), is analogous to that in Blicke v. Treves, 241 F.2d at 720-21, 112 USPQ at 475. In the Blicke case, Blicke urged that making the new compounds in issue, without testing, was sufficient to establish a reduction to practice because the compounds, which were said to be antispasmodic agents, in the Blicke application, were “of a kind known to be

antispasmodics". The court disagreed and held that tests were required. It said:

It is evident that, while the antispasmodic properties of a new material might be reasonably deduced from its similarity to known antispasmodics, they could not be foretold with certainty; and that fact is apparent from the record here which shows that appellant and his associates subjected the new material to very extensive tests.

For the reasons given, we hold that the instant compounds are not of such a nature that they were reduced to practice merely by making them. Id. at 475.

In the instant case, A-79935 is a novel compound said to have pharmacological activity as a 5-LO inhibitor. However, it has not been shown that 5-LO inhibitor activity could have been "foretold with certainty" based on structural similarity of A-79935 to other known N-hydroxyurea and hydroxamic compounds, known as 5-LO inhibitors. Kreft's assertion that the N-hydroxyurea and hydroxamic acid portion of the molecule is responsible for 5-LO inhibitor activity is not supported by evidence. It is not sufficient to establish a reduction to practice for an expert to assert an opinion that one of ordinary skill in the art would have expected a novel compound to have practical utility based on structural similarity. Blicke, 241 F.2d at 720-21, 112 USPQ at 475. Kreft alleges that "hydrophobicity" is a common property of the known N-hydroxyurea and hydroxamic acid 5-LO inhibitors and A-79935. However, Brooks have not pointed to any evidence to establish that "hydrophobicity" is a significant property contemporaneously uncovered and appreciated by Brooks which is common to both compound A-79935 and other known 5-LO inhibitors and that such knowledge of this specific property would lead one of ordinary skill in the art to foretell with certainty that A-79935 is useful as a 5-LO inhibitor. See Ciric,

511 F.2d at 1185, 185 USPQ at 105, and In re Folkers, 344 F.2d 970, 974, 145 USPQ 390, 393 (Fed. Cir. 1965) (Usefulness of a compound is invariably a manifestation of a given property of that compound and some uses can be immediately inferred from a recital of certain properties). Accordingly, we hold that A-79935 was not reduced to practice when it was prepared; rather, testing to establish a practical utility was necessary.

The reliance on coinventor Brooks' testimony is misplaced. His testimony as to what he believed when he made the entry, "5-LO", in his notebook, does not establish an actual reduction practice but at best constitutes evidence of conception of utility. Rey-Bellet, 493 F.2d at 1385-86, 181 USPQ at 457 (conception of NTL as an antidepressant by the inventor is sufficient to complete the conception of utility because nothing beyond the exercise of routine skill would have been required to demonstrate that it had this activity.)

Brooks argue that during the prosecution of each of the involved applications and in the interference, no one ever stated that 5-LO inhibitory activity would not have been expected. This argument is not persuasive. The standard used for determining whether an application satisfies 35 U.S.C. §101 and/or 35 U.S.C. §112 as to a sufficiently specific use differs from the standard used in evaluation of whether the practical utility requirement has been satisfied in proving a reduction to practice of a novel compound. An expectation that a compound possesses a certain property does not establish that practical utility of that compound could be foretold with certainty. A novel compound does not

have an established utility and thus testing must occur to establish practical utility.

Brooks argue that for determining whether practical utility has been demonstrated, the relevant person is “one of skill in the art” not “one of ordinary skill in the art.”(original emphasis) This argument is not persuasive. In our view, “one of skill in the art” and “one of ordinary skill in the art” are one and the same person(s).

Brooks' contend that “[A]ll that is required for actual reduction to practice is that it be shown that it be ‘reasonably certain’ that the subject matter will perform its intended function in actual service...” Gellert v. Wamberg, 495 F.2d 779, 782-83, 181 USPQ 648, 651 (CCPA 1974) , citing Chittick v. Lyons, 104 F.2d 818, 820, 42 USPQ 132 , 134 (CCPA 1939)(emphasis added in Gellert).(BB-42) Brooks' reliance on the decisions of Gellert and Chittick is misplaced. In the instant interference, no testing was conducted before the critical date, whereas in Gellert and Chittick tests were in fact conducted on the constructed embodiments and from the test results it was concluded that one of ordinary skill would be “reasonably certain” that the invention would have worked as intended. The reasonableness standard in determining practical utility addresses whether the testing conducted is sufficient to prove usefulness, not whether utility is obvious or would have been expected without testing.

For the foregoing reasons, we hold that Brooks et al. have not established a reduction to practice of the subject matter of the count, and thus Ikeda et al, as senior party, must prevail.

Interference No. 103378

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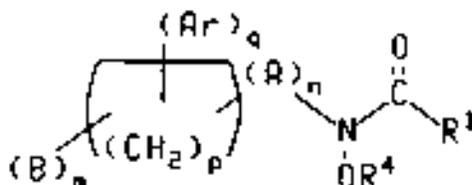
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MFD/dal

APPENDIXCount 3

A compound having the structure



or a pharmaceutically acceptable salt thereof wherein:

R4 is hydrogen, aroyl, C1 to C6 alkoyl, a pharmaceutically acceptable cation or metabolically cleavable group;

R1 is hydrogen, C1 to C12 alkyl, C2 to C4 alkenyl, C3 to C8 cycloalkyl, alkylthioalkyl, alkoxyalkyl or -NR2R3;

R2 and R3 are each independently hydrogen, hydroxy, C1 to C6 alkyl, C1 to C6 hydroxyalkyl, C2 to C8 alkanoyl, alkoxyalkyl in which the alkoxy portion and the alkyl portion each contain, independently, from 1 to 6 carbon atoms, aryl or aryl substituted with one or more substituents selected from the group consisting of halo, nitro, cyano, C1 to C12 alkyl, C1 to C12 alkoxy, C1 to C12 halosubstituted alkyl, C1 to C12 hydroxysubstituted alkyl, C1 to C12 alkoxy carbonyl, aminocarbonyl, C1 to C12 alkylaminocarbonyl, di C1 to C12 alkylaminocarbonyl and C1 to C12 alkylsulfonyl, provided that R2 and R3 are not both hydroxy;

A is C1 to C6 alkylene or C2 to C6 alkenylene;

B is independently, halo, nitro, cyano, -SH, hydroxy, C1 to C6 alkyl, C1 to C6 alkoxy, C1 to C6 halosubstituted alkyl, C1 to C6 thioalkyl, C2 to C6 alkenyl, C1 to C12 aminocarbonyl, C1 to C6 alkylaminocarbonyl, di C1 to C6 alkylaminocarbonyl or C2 to C12 alkoxyalkyl;

Ar is

- a) C5 to C20 alkyl
- b) C3 to C8 cycloalkyl
- c) optionally substituted carbocyclic aryl
- d) optionally substituted carbocyclic

- aryl)cycloalkyl(C3-C8)
- e) optionally substituted (carbocyclic aryl) alkyl (C1-C6)
- f) optionally substituted carbocyclic aryloxyalkyl(C1-C6)
- g) optionally substituted (carbocyclic aryl) alkoxy (C1-C6)alkyl(C1-C6)
- h) optionally substituted carbocyclic arylthioalkyl(C1-C6)

wherein the optional substituents on the carbocyclic aryl groups are selected from the group consisting of:

hydroxy, halo, nitro, cyano, C1 to C12 hydroxysubstituted alkyl, C1 to C12 alkylamino, di C1 to C12 alkylamino, aminocarbonyl C1 to C12 alkoxy carbonyl, C1 to C12 alkylaminocarbonyl, di C1 to C12 alkylaminocarbonyl and C1 to C12 alkylsulfonyl;

C1 to C12 alkyl,
C1 to C12 alkoxy,
C1 to C12 haloalkyl,
(C1-C6)alkoxy(C1-C6),

phenyl, optionally substituted with C1-C6 alkyl, C1-C6 haloalkyl and C1-C6 alkoxy, hydroxy or halogen,

phenoxy, optionally substituted with C1-C6 alkyl, C1-C6 haloalkyl, C1-C6 alkoxy or halogen,

phenylthio, optionally substituted with C1-C6 alkyl, C1-C6 haloalkyl, C1-C6 alkoxy or halogen,

2-,3- or 4-pyridyl, optionally substituted with C1-C6 alkyl, C1-C6 haloalkyl, C1-C6 alkoxy or halogen,

2-,3- or 4-pyridyloxy, optionally substituted with C1-C6 alkyl, C1-C6 haloalkyl, C1-C6 alkoxy or halogen,

i) 2- or 3-furyl or 2- or 3-thienyl, optionally substituted with hydroxy, halo, nitro, cyano, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 haloalkyl, C1-C12 hydroxyalkyl, C1-C12 alkylamino, di C1-C12 alkylamino, C1-C12 alkoxy carbonyl, aminocarbonyl, C1-C12 alkylaminocarbonyl, di C1-C12 alkylaminocarbonyl C1-C12 alkylsulfonyl and phenyl, phenoxy, phenylthio, 2-,3- or 4-pyridyl, 2-,3-,4-pyridyloxy further optionally substituted with C1-C6 alkyl, C1-C6 haloalkyl, C1-C6 alkoxy or halogen,

j) benzo[b]furyl or 2- or 3-benzo[b]thienyl, optionally substituted with C1-C6 alkyl, C1-C6 haloalkyl, C1-C6 alkoxy or halogen, and

k) quinoyl, optionally substituted with hydroxy, halo, nitro, cyano, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 haloalkyl, C1-C12 hydroxyalkyl, C1-C12 alkylamino, di C1-C12 alkylamino, C1-C12 alkoxy carbonyl, aminocarbonyl, C1-C12 alkylaminocarbonyl, di C1-C12 alkylaminocarbonyl and C1-C12 alkylsulfonyl;

Ar and B, together with the carbon atoms to which they are attached, may form a ring;

n is 0 or 1;

m is 0 to 3;

p is 2 to 6; and

q is 1 or 2;

or

a pharmaceutical composition comprising a therapeutically effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

or

a method of inhibiting the biosynthesis of leukotrienes comprising administering to a mammal in need of such a treatment a therapeutical effective amount of a compound of formula I.

The claims corresponding to count 3 are as follows:

Brooks: claims 1-11.

Hodgson: claims 1-7, 11-17, 21-34.

Ikeda: claims (as amended) 1-10, 13-19, 23-24, 27-28 and 32.