

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 52

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte SHOW-CHU WONG and SYLVIA KHOO

Appeal No. 2002-1629
Application No. 08/863,121

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 25-29, all of the claims remaining. Claim 25 is representative and reads as follows:

25. A multi-purpose, cyanide-free lyse reagent for making hemoglobin (Hb) and leukocyte (WBC) determinations comprising, in combination;

(a) an aqueous multipurpose lyse reagent comprising at least one quaternary ammonium salt, said quaternary salt selected from the group consisting of: tetradecyltrimethyl ammonium bromide (TTAB), dodecyltrimethyl ammonium chloride, cetyl trimethyl ammonium bromide, hexadecyltrimethyl ammonium bromide, benzalkonium chloride, cetylpyridium chloride, and

(b) at least one hydroxylamine salt selected from the group consisting of: hydrochloride, sulfate, phosphate, and other acid salts; wherein said multipurpose lyse reagent produces a chromogen having maximum absorbance between 530 and 550 nm.

The examiner relies on the following references:

Ledis et al. (Ledis)	4,485,175	Nov. 27, 1984
Toda et al. (Toda)	5,250,437	Oct. 05, 1993
Narayanan et al. (Narayanan)	5,336,518	Aug. 09, 1994

Bunn et al. (Bunn), "Hemoglobin: Molecular, Genetic and Clinical Aspects," W.B. Saunders Company, pp. 638-644 (1986)

Claims 25, 26, and 28 stand rejected under 35 U.S.C. § 103 as obvious in view of Toda, Ledis, and Bunn.

Claims 27 and 29 stand rejected under 35 U.S.C. § 103 as obvious in view of Toda, Ledis, Bunn, and Narayanan.

We reverse.

Background

The "standard methods for determining white blood cell (WBC) counts and hemoglobin (Hb) determinations traditionally utilize reagents containing potassium cyanide (KCN) or other cyanide containing compounds. These cyanide compounds can be hazardous to use because they can produce toxic hydrogen cyanide (HCN)." Specification, page 1. The standard reagent used in automated hematology instruments "typically contains ingredients to properly lyse the erythrocytes to permit accurate leukocyte counting, and a cyanide containing compound for the formation of a stable chromogen (cyanmethemoglobin) to

enable precise colorimetric analysis of the hemoglobin content in the erythrocytes.” Id., page 2.

The specification discloses “cyanide-free reagents for use in the rapid formation of a stable and detectable chromogen which is indicative of the amount of hemoglobin present in a whole blood sample by conventional methodology.”

Page 1. The disclosed reagents comprise one of several specified quaternary ammonium salts together with a hydroxylamine salt. See, e.g., page 3.

Discussion

Claim 25, the broadest claim on appeal, is directed to a “cyanide-free lyse reagent” comprising at least one of certain quaternary ammonium salts in combination with at least one of several hydroxylamine salts. Claim 25 also specifies that the “reagent produces a chromogen having maximum absorbance between 530 and 550 nm.”

The examiner rejected claims 26, 26, and 28 as obvious in view of Toda, Ledis, and Bunn, and rejected claims 27 and 29 over those references further combined with Naranayan. Since both rejections rely on the combination of Toda, Ledis, and Bunn, we can consider them together.

The examiner characterized Toda as “teach[ing] an aqueous cyanide free hemoglobin and leukocyte reagent which includes at least one quaternary ammonium salt [albeit not one of those recited in the instant claims], . . . and an oxidant capable of oxidizing heme in hemoglobin, such as sodium nitrite.”

Examiner’s Answer, page 5. He acknowledged that Toda “does not teach

hydroxylamine as the oxidant and does not teach the particular quaternary ammonium salt combinations.” Id.

The examiner cited Ledis as disclosing the particular quaternary ammonium salt(s) recited in the claims, and relied on Bunn as “teach[ing] that hydroxylamine is an alternative to oxidants such as ferricyanide and nitrites in the oxidation of hemoglobin, see page 642, Table 16-3 and the addendum thereto regarding nitrites.” Examiner’s Answer, page 5. He concluded that it would have been obvious to use Ledis’ quaternary ammonium salts in Toda’s method, and that

[i]t would have been further obvious to the ordinarily skilled artisan at the time the invention was made to have used hydroxylamine in lieu of the sodium nitrite or other suggested oxidants as the oxidant capable of oxidizing heme in hemoglobin in Toda et al., as modified, in view of the known equivalent function of hydroxylamine, nitrite, or other oxidants for the oxidation of hemoglobin as taught in Bunn et al. and because the selection of any of these known equivalents for oxidizing hemoglobin would have been within the level of ordinary skill in the art absent a showing of unexpected results.

Examiner’s Answer, page 6.

“In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. ‘[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.’” In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citations omitted). “Only if that burden is met, does

the burden of coming forward with evidence or argument shift to the applicant.”
In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993).

In this case, we conclude that the examiner has not adequately shown that a person of ordinary skill in the art would have been motivated to combine the hydroxylamine taught by Bunn with the quaternary ammonium salts taught by Toda and Ledis. Bunn discloses that hydroxylamine is one of several agents that directly oxidize hemoglobin (Table 16-3, page 642). Bunn also discloses that nitrites, among other agents, oxidize hemoglobin via interaction with oxygen. See id.

The examiner concluded that this disclosure would have led those skilled in the art to view hydroxylamine and nitrites as “known equivalents.” The examiner also relied on Toda’s teaching that a quaternary ammonium salt is combined with an oxidizing agent selected from the group consisting of “nitrite ion, quinone compound, alloxan, methylene blue, aniline, acetanilide, nitrobenzene, acetophenetidin, nitrotoluene, sulfonamide, phenylhydrazine, ascorbic acid or aminophenol.” Col. 3, lines 59-62. See the Examiner’s Answer, page 9. Taken together, in the examiner’s view, these disclosures would have suggested substituting hydroxylamine for the sodium nitrite used by Toda, to a person of ordinary skill in the art.

We disagree. “Most if not all inventions arise from a combination of old elements. Thus, every element of a claimed invention may often be found in the prior art. However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. Rather, to

establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant.” In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000).

An adequate showing of motivation to combine requires “evidence that ‘a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.’” Ecolochem, Inc. v. Southern Calif. Edison Co., 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075 (Fed. Cir. 2000). To support a case of prima facie obviousness, “particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.” In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000).

Here, we conclude that the examiner has not adequately shown that a person skilled in the art, with no knowledge of the present disclosure, would have been motivated to substitute hydroxylamine for the other oxidizing agents known in the art. It is true that Bunn teaches that both hydroxylamine and nitrites oxidize hemoglobin. However, Bunn also teaches a variety of other agents that have the same effect. See Table 16-3, page 642: Bunn discloses that some agents directly oxidize hemoglobin (ferricyanide, copper, hydrogen peroxide, hydroxylamine, chromate, chlorate, nitrogen trifluoride, tetranitromethane, quinones, and dyes); some agents oxidize hemoglobin via interaction with

oxygen (nitrites, hydrazines, thiols, arsine, aminophenols, arylhydroxylamines, N-hydroxyurethane, phenylenediamines); and some agents oxidize hemoglobin via biochemical transformation (anilines, sulfanilamide, 4,4'-diaminodiphenylsulfone, the 8-aminoquinolines primaquine and pamaquine, and the N-acylarylamines acetanilid and phenacetin).

Neither Bunn nor the other references cited by the examiner provide a suggestion or motivation to choose hydroxylamine, from all the compounds disclosed by Bunn, and substitute it into the method disclosed by Toda. Granted, Toda notes that problems arise from using cyanide-containing solutions in automatic blood analyzers (col. 1, lines 45-61) and suggests the use of non-cyanide oxidizing agents (col. 3, lines 59-62). However, the agents suggested by Toda as substitutes for cyanide do not include the hydroxylamine recited in the instant claims.

The examiner has pointed to nothing in either Toda or the other references that would have suggested substituting hydroxylamine for the agents suggested by Toda. Since the cited references can only be combined with the benefit of hindsight, they do not support a prima facie case of obviousness. The rejections under 35 U.S.C. § 103 are reversed.¹

¹ The rejection of claims 27 and 29 relies on the same rationale, with an additional reference being added to meet the specific limitations of these claims. Thus, our reversal of the rejection based on Toda, Ledis, and Bunn requires reversal of both rejections on appeal.

Summary

The examiner has not shown that a person of ordinary skill in the art would have been motivated to combine the cited references. Therefore, we reverse the rejections under 35 U.S.C. § 103.

REVERSED

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