

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 41

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte HAZEM EL-REFAEY

Appeal No. 2002-0546
Application No. 08/809,379

ON BRIEF

Before MILLS, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, 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 15 and 16, which read as follows:

15. A method of limiting postpartum hemorrhage comprising administering orally a single effective dose of misoprostol to a woman during the third stage of labor.
16. A method of limiting postpartum hemorrhage comprising administering by pessary or suppository a single effective dose of misoprostol to a woman during the third stage of labor.

The examiner relies upon the following references:

Symonds, "The Third Stage of Labor," Essential Obstetrics and Gynaecology, pp. 108-109 (1987)

Facts and Comparisons, pp. 117h-118, and 118a (1990)

Sanchez-Ramos et al. (Sanchez-Ramos), "Labor Induction With the Prostaglandin E₁ Methyl Analogue Misoprostol Versus Oxytocin: A Randomized Trial," Obstet Gynecol, Vol. 81, pp. 332-336 (1993)

Campos et al. (Campos), "Misoprostol – An Analog of PGE₁ – for the Induction of Labor at Term: Comparative and Randomized Study with Oxytocin," Revista Chilena de Obstetricia y Ginecologia, Vol. LIX, No. 3, pp. 190-196 (1994)

Sherwen et al., Maternity Nursing: Care of the Childbearing Family, 3rd Ed., pp.676-679, 749-750, 760-761, and 871-872 (1999)

The claims stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Campos, Sanchez-Ramos, Facts and Comparisons, Maternity Nursing, and Symonds. After careful review of the record and consideration of the issue before us, we reverse.

DISCUSSION

Claims 15 and 16 have been rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Campos, Sanchez-Ramos, Facts and Comparisons, Maternity Nursing, and Symonds.

Campos and Sanchez-Ramos are cited for teaching "that misoprostol is known to be useful orally and intravaginally to cause uterine contractions and induce labor (antepartum)." Examiner's Answer, page 4. The rejection acknowledges that "[t]he claims differ in that they are drawn to methods of limiting postpartum hemorrhage comprising administering misoprostol orally and

intravaginally in the third stage of labor,” i.e., administering misoprostol postpartum.

Facts and Comparisons, according to the statement of the rejection, “teaches that an agent known to cause uterine contractions and thereby induce labor antepartum, is also known to be useful at increased dosages to cause uterine contractions and thereby treat hemorrhaging post partum when firm, tetanic contractions are known to be beneficial.” Id. at 4. Symonds is cited for teaching that the postpartum stages of labor include the third and fourth stages, and that these stages may last up to six hours after delivery. See id.

The rejection concludes:

One of ordinary skill in the art would have found it obvious to employ any agent known to cause uterine contractions antepartum to treat postpartum hemorrhaging since the agent would be expected to cause the firm, tetanic contractions known to be beneficial postpartum to control hemorrhaging when administered at an increased dosage.

Examiner’s Answer, pages 4-5.

Appellant argues that “the combination of [the] prior art of record in this case fails to provide any reasonable expectation of success that oral administration of misoprostol or administration of misoprostol via pessary or suppository during the third stage of labor would be effective at inhibiting postpartum hemorrhaging.” Appeal Brief, page 8.

Appellant asserts that just because a single agent, oxytocin, has been shown to be useful in the first and second stages of labor, as well as the third stage, the art provides no reasonable expectation that misoprostol, a different

agent, would act similarly. In addition, another agent, methylergonivine maleate, while useful in the third stage of labor, is contraindicated in the first and second stages. See id. at 10.

Appellant also contends that the ability of misoprostol to inhibit uterine bleeding was unexpected. Appellant cites the Physician' Desk Reference (1999) (PDR), which contraindicates the use of misoprostol in pregnant women. See id. at 11-12.

The burden is on the examiner to make a prima facie case of obviousness, and the examiner may meet this burden by demonstrating that the prior art would lead the ordinary artisan to combine the relevant teachings of the references to arrive at the claimed invention. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988). Obviousness is determined in view of the sum of all of the relevant teachings in the art, not isolated teachings in the art. See In re Kuderna, 426 F.2d 385, 389, 165 USPQ 575, 578 (CCPA 1970); see also In re Shuman, 361 F.2d 1008, 1012, 150 USPQ 54, 57 (CCPA 1966). In assessing the teachings of the prior art references, the examiner should also consider those disclosures that may teach away from the invention. See In re Geisler, 116 F.3d 1465, 1469, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997).

As noted by the examiner, both Campos and Sanchez-Ramos teach the use of misoprostol to induce labor at term. While both references compare the effects of misoprostol to oxytocin, neither reference suggests that misoprostol may be administered in the third stage of labor to limit postpartum hemorrhaging.

Facts and Comparisons discusses the actions and indications of oxytocin. The reference teaches that oxytocin “produce[s] uterine contractions during the third stage of labor and [] control[s] postpartum bleeding or hemorrhage.” Id. at 177h. It also states that oxytocin may be administered intravenously or intramuscularly for the control of postpartum uterine bleeding. See id. at 118a.

Maternity Nursing notes that “[d]uring the early postpartum period, pharmacologic agents may be used to promote uterine contractions and consequently minimize uterine bleeding.” Id. at 871. The reference discusses the use of methylergonovine maleate to control postpartum bleeding, but also notes that it should not be used to induce labor. See id. at 872.

We agree with appellant that the combination provides no reasonable expectation of success of using misoprostol in the third stage of labor to prevent postpartum hemorrhaging. If one were to interpret the art as suggested by the rejection, one of ordinary skill would expect agents that produce uterine contractions to be useful both antepartum for the induction of labor and postpartum for the control of hemorrhaging. But as taught by Maternity Nursing, while the agent methylergonovine maleate may be used control postpartum bleeding, its use is contraindicated for the induction of labor. Therefore, the prior art demonstrates that there is no reasonable expectation of success of using any agent that induces uterine contractions for the induction of labor, and thus also demonstrates that there is no reasonable expectation of success of using any agent that induces uterine contractions for the control of postpartum hemorrhaging.

Furthermore, the PDR notes that cytotec (misoprostol) “caused partial or complete expulsion of the uterine contents in 11% of the subjects and increased uterine bleeding in 41%” in women undergoing an elective termination of their pregnancy in the first trimester. Thus, appellant asserts that the ability of misoprostol to decrease uterine bleeding is unexpected because of its known liability of causing uterine bleeding. See Appeal Brief, page 11.

In response, the examiner asserts that

[t]he liability of misoprostol, noted in the [PDR] to cause uterine bleeding and miscarriage in some woman (making its use in pregnant women undesirable) would be reasonably expected to be avoided by the administration of a dosage of this agent which is greater than in the prior art.

Examiner’s Answer, page 9. The examiner, however, provides no supporting documentation or evidence to support the contention that one would expect side effects of the drug, such as increased uterine bleeding, to decrease at increased dosages of the drug. See, e.g., In re Lee, 277 F.3d 1338, 1343-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (in reviewing an obviousness rejection, the court noted that “conclusory statements” as to teaching, suggestion or motivation to arrive at the claimed invention “do not adequately address the issue.”).

CONCLUSION

Because the rejection fails to provide a reasonable expectation of success of using misoprostol in the control of postpartum hemorrhaging when administered during the third stage of labor, it is reversed.

REVERSED

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| Demetra J. Mills |) | |
| Administrative Patent Judge |) | |
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| |) | BOARD OF PATENT |
| Eric Grimes |) | |
| Administrative Patent Judge |) | APPEALS AND |
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