

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte LEONARD L. MAZUR

Appeal No. 2004-0394
Application No. 09/915,467¹

ON BRIEF

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-3 and 5-10. The examiner objected to the remaining claim, claim 4, as dependent upon a rejected base claim.

Claims 1 and 6 are illustrative of the subject matter on appeal and are reproduced below:

1. An educational article of manufacture useful to increase patient awareness of the teratogenicity of a pharmaceutical, said article of manufacture comprising: a teratogenic pharmaceutical packaged together with a contraceptive; and labeling specifying avoidance of pregnancy while using said teratogenic pharmaceutical.

¹ We note appellant's petition to make special (Paper No. 3), accordingly we have taken this Appeal out of order.

6. A pharmaceutical composition of matter comprising:
a first pharmaceutical in an amount potentially teratogenic, and
a second pharmaceutical in an amount effective as a contraceptive,
said composition of matter in a unit dose form.

The references relied upon by the examiner are:

Gaull	4,545,977	Oct. 8, 1985
Nedberge et al. (Nedberge)	4,816,258	Mar. 28, 1989
Abrams et al. (Abrams) (102(e) date Aug. 18, 1999)	6,428,809	Aug. 6, 2002

GROUND OF REJECTION

Claims 1-3, 5, 6, 8 and 9 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Abrams.

Claims 6 and 7 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Nedberge.

Claims 1-3, 5, 6 and 8-10 stand rejected under 35 U.S.C. § 103 as being unpatentable over Abrams in view of Gaull.

Because in our opinion, a picture speaks a thousand words, we vacate the pending rejections in favor of the following new grounds of rejection under 37 CFR § 1.196(b).

NEW GROUNDS OF REJECTION

According to appellant's specification (page 7),

the term 'teratogenic' ... include[s] pharmaceuticals associated with an increased risk of birth defects. The term thus includes pharmaceuticals with FDA-approved labeling citing an increased risk of birth defects as a potential side effect. Such teratogenic pharmaceuticals currently listed in the PHYSICIANS' DESK REFERENCE (Medical Economics Company, publ. 2000) include, for example, isotretinoin (ACCUTANE®)....

Claims 1, 2, and 5:

As set forth above, claim 1 is drawn to an article of manufacture, wherein a teratogenic pharmaceutical is packaged together with a contraceptive. Claim 2 depends from claim 1 and requires that the teratogenic pharmaceutical is isotretinoin. Claim 5, also depends from claim 1 and requires that the contraceptive is a pharmaceutical in an amount effective as a contraceptive.

According to Elsayed² (column 1, lines 48-57),

Previous methods for controlling the distribution of drugs have been developed in connection with Accutane (isotretinoin). Accutane, which is a known teratogen, is a uniquely effective drug for the treatment of severe, recalcitrant, nodular acne. A pregnancy prevention program was developed, and the Slone Epidemiology Unit of Boston University designed and implemented a survey to evaluate these efforts. The survey identified relatively low rates of pregnancy during Accutane treatment, which suggests that such a program can be effective.

Furthermore, Elsayed discloses (column 3, lines 26-31),

Generally speaking, the methods of the present invention may be desirably and advantageously used to educate and reinforce the actions and behaviors of patients who are taking the drug, as well as prescribers who prescribe the drug and pharmacies which dispense the drug. ... A wide variety of educational materials may be employed to ensure proper prescribing, dispensing and patient compliance according to the methods described herein, including, for example, a variety of literature and other materials, such as, for example, product information, educational brochures, continuing education monographs, videotapes and the like which may describe the risks and benefits associated with taking the particular drug.

Consistent with Elsayed's emphasis on education, Elsayed discloses (column 9, lines 21-29),

The drug is preferably supplied to the pharmacy (as well as the patient) in packaging, such as individual blister packs, which includes warnings regarding the risks associated with the drug, as well as the importance of various aspects of the present methods such as, for example, pregnancy testing and the use of contraception (in the case of teratogenic drugs),

² Elsayed et al. (Elsayed)
(102(e) date Aug. 28, 1998)

and the dangers associated with sharing the drug with others, among other aspects.

In this regard, we note that the last two steps (step g and step h) of the Elsayed method require (step g) pharmacies to fill prescriptions for non-pregnant patients, and (step h) provide patients who are capable of becoming pregnant a contraceptive device or formulation. See e.g., Elsayed, claim 1 and claim 10.

Consistent with Elsayed, we note that according to the PDR³, page 1878, second column 2:

The following text is [the] complete prescribing information based on official labeling in effect June 1, 1991.

Avoid Pregnancy



CONTRAINDICATION AND WARNING
Accutane must not be used by females who are pregnant or who may become pregnant while undergoing treatment. There is an extremely high risk that a deformed infant will result if pregnancy occurs while taking Accutane in any amount even for short periods. Potentially all exposed fetuses can be affected. Accutane is contraindicated in women of childbearing potential unless the patient meets all of the following conditions:

- has severe disfiguring cystic acne that is recalcitrant to standard therapies
- is reliable in understanding and carrying out instructions
- is capable of complying with the mandatory contraceptive measures
- has received both oral and written warnings of the hazards of taking Accutane during pregnancy and the risk of possible contraception failure and has acknowledged her understanding of these warnings in writing
- has had a negative serum pregnancy test within two weeks prior to beginning therapy (It is also recommended that pregnancy testing and contraception counseling be repeated on a monthly basis. To encourage compliance with this recommendation, the physician should prescribe no more than a one month supply of the drug.)
- will begin therapy only on the second or third day of the next normal menstrual period

Major human fetal abnormalities related to Accutane administration have been documented: CNS abnormalities (including cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit); skull abnormality; external ear abnormalities (including anotia, micropinna, small or absent external auditory canals); eye abnormalities (including microphthalmia); cardiovascular abnormalities; facial dysmorphism; thymus gland abnormality; parathyroid hormone deficiency. In some cases death has occurred with certain of the abnormalities previously noted. Cases of IQ scores less than 85 with or without obvious CNS abnormalities have also been reported. There is an increased risk of spontaneous abortion. In addition, premature births have been reported.

Effective contraception must be used for at least one month before beginning Accutane therapy, during therapy, and for one month after the last dose. The physician and patient should discuss the desirability of continuing the pregnancy.

Accutane should be prescribed only by physicians who have special competence in the diagnosis and treatment of severe recalcitrant cystic acne, are experienced in the use of systemic retinoids and understand the risk of severe birth defects. It should not be used during pregnancy.

As set forth in the above labeling information (PDR 1878, column 2), “Accutane must not be used by females who are pregnant or who may become pregnant while

³ Physicians’ Desk Reference (PDR) 1978-1980 (46th ed., Medical Economics Company, Montvale, NJ 1992).

undergoing treatment.” In addition, the labeling information recommends (*id.*), “that two reliable forms of contraception be used simultaneously unless abstinence is the chosen method.” We find the labeling information educational in that it specifies, by text and illustration, that one should avoid pregnancy while using Accutane (isotretinoin).

In our opinion, given the recognized danger of becoming pregnant while taking isotretinoin, a person of ordinary skill in the art would have been motivated to package⁴ isotretinoin together with a contraceptive. In this regard, we note that Abrams, recognized that “[i]sotretinoin and analogs and isomers used for the treatment of postular acne has a severe danger if taken by a woman who [is] pregnant,” and therefore teaches, “[t]he incorporation of oral contraceptive medication would eliminate the potential for pregnancy^[5] while medicated.” Note, by way of illustration, that claim 11 of Abrams is drawn to “[a] pharmaceutical delivery package comprising a mixture of [i]sotretinoin and an oral contraceptive.”

In our opinion, Abrams provides a person of ordinary skill in the art with the motivation to package isotretinoin together with a contraceptive. “The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art.” In re Keller, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). Based on the evidence set forth above, we find that it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to package a contraceptive formulation and/or device together with isotretinoin (Accutane), and label said composition according to the official labeling information set forth in the PDR.

⁴ We note that appellant defines “packaged together” as “a unitary package for sale as an undivided unit.” See appellant’s Specification, page 9.

We are not persuaded by appellant's assertion (Reply Brief, page 3), Abrams, "teaches an article of manufacture which assures, by definition, that the contraceptive will be used. In contrast, the S[pecification] notes, 'this article of manufacture does not assure the contraceptive will in fact be used...'" As discussed above, each limitation of the claimed invention is taught by the combination of references relied upon.

Furthermore, as discussed above, in our opinion, the combination of references relied upon would motivate a person of ordinary skill in the art to package isotretinoin together with a contraceptive. Therefore, based on this evidence, it is our opinion that it would have been prima facie obvious to a person of ordinary skill in the art, at the time the invention was made, to package isotretinoin together with a contraceptive and to label the package according to the PDR specifying that one should avoid becoming pregnant while taking isotretinoin.

Accordingly, claims 1, 2, and 5 are rejected under 35 U.S.C. § 103 as being unpatentable over the combination of Elsayed, Abrams and PDR.

Claims 3 and 4:

Claim 3 depends from claim 1 and requires that the contraceptive comprise a device. Claim 4 depends from, and further limits claim 3 to an intrauterine device.

As set forth above, based on the combination of Elsayed, Abrams and PDR, we find that it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to package a contraceptive together with isotretinoin (Accutane), and label said composition according to the official labeling information set forth in the PDR. While Abrams discloses the incorporation of the contraceptive medication together with isotretinoin, Elsayed provides patients with a contraceptive

⁵ We understand this phrase to mean that the contraceptive would be in an amount effective as a contraceptive.

device or formulation. In our opinion, based on this evidence, a person of ordinary skill in the art would have been motivated to package isotretinoin together with a contraceptive medication, a contraceptive device or as recommended by the PDR (“two reliable forms of contraception”), both a contraceptive medication and a device. Keller.

This combination of references, however, does not specifically teach an intrauterine device. To make up for this deficiency, we note that Van Os⁶ teach an intrauterine contraceptive device. As Van Os discloses (column 2, lines 1-5), the intrauterine device overcomes or reduces the disadvantages associated with bleeding and pain of other intrauterine contraceptive devices. Therefore, in our opinion, a person of ordinary skill in the art would have been motivated to use the intrauterine contraceptive device disclosed by Van Os for the benefits disclosed therein. In our opinion, based on this evidence, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the invention was made, to use the intrauterine contraceptive device disclosed by Van Os as the contraceptive device taught by Elsayed.

Accordingly, claims 3 and 4 are rejected under 35 U.S.C. § 103 as being unpatentable over the combination of Elsayed, Abrams and PDR in view of Van Os.

Claims 6, and 8-10:

As set forth above, claim 6 is drawn to a unit dose form of a pharmaceutical composition comprising a first pharmaceutical in an amount potentially teratogenic, and a second pharmaceutical in an amount effective as a contraceptive. Claim 8 depends from, and further limits claim 6 to a unit dose form that is administered orally. Claim 9, depends from, and further limits the teratogenic pharmaceutical of claim 8 to

⁶ Van Os et al. (Van Os)

isotretinoin. Claim 10, depends from, and further limits claim 9 to an amount of isotretinoin of about 5 mg to about 40 mg per dose.

As set forth above, based on the combination of Elsayed, Abrams and PDR, we find that it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to package a contraceptive together with isotretinoin (Accutane), and label said composition according to the official labeling information set forth in the PDR. Furthermore, as discussed above, Abrams, recognized that “[i]sotretinoin and analogs and isomers used for the treatment of postular acne has a severe danger if taken by a woman who [is] pregnant,” and therefore teaches, “[t]he incorporation of oral contraceptive medication would eliminate the potential for pregnancy while medicated.” Note again, by way of illustration, that claim 11 of Abrams is drawn to “[a] pharmaceutical delivery package comprising a mixture of [i]sotretinoin and an oral contraceptive.” In our opinion, Abrams provides a person of ordinary skill in the art with explicit motivation to combine isotretinoin together with a contraceptive in a unit dose form. Regarding the amount of isotretinoin per dose, we note that the PDR teaches (page 1878, column 3), “Accutane ... is available in 10-mg, 20-mg and 40-mg soft gelatin capsules for oral administration.”

To the extent that appellant argues (Brief, page 8), and the declaration of Engle asserts (Paper No. 10), that Abrams is not enabled for the electrostatic transfer of a wax, we note that as an alternative to electrostatic transfer the powder, or assuming arguendo the wax, “may be placed directly onto the membrane.” See Abrams, column 4, lines 63-64. As Abrams illustrates in Figures 4 and 5, and discusses (column 6, lines 1-8), multi-drug formulations can be made according to the disclosed method.

Therefore, based on this evidence, it is our opinion that it would have been prima facie obvious to a person of ordinary skill in the art, at the time the invention was made, to combine isotretinoin together with a contraceptive and to label the package according to the PDR specifying that one should avoid becoming pregnant while taking isotretinoin. Accordingly, claims 6, and 8-10 are rejected under 35 U.S.C. § 103 as being unpatentable over the combination of Elsayed, Abrams and PDR.

Claim 7:

As set forth above, based on the combination of Elsayed, Abrams and PDR, we find that it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to package a contraceptive formulation or device together with isotretinoin (Accutane), and label said composition according to the official labeling information set forth in the PDR. This combination of reference, however, does not specifically teach transdermal administration of a pharmaceutical composition comprising isotretinoin and a contraceptive. To make up for this deficiency, we note that Hansen⁷ teach a “transdermal delivery system comprising one or more active substances” selected from the group including “contraceptive agents” and “isotretinoin.” See Hansen, column 5, line 51 – column 6, line 37, particularly column 6, lines 21-23 for contraceptive agents, and column 6, line 36 for isotretinoin.

In our opinion, Hansen provides an alternative (transdermal administration) to Abrams’ disclosure of a “unitary pill” (see e.g., Brief, page 4) for oral administration. Based on this evidence, it is our opinion that it would have been prima facie obvious to a person of ordinary skill in the art to use the transdermal system disclosed by Hansen to administer isotretinoin together with a contraceptive. Accordingly, claim 4 is rejected

⁷ Hansen et al. (Hansen)

under 35 U.S.C. § 103 as being unpatentable over the combination of Elsayed, Abrams and PDR in view of Hansen.

LONG FELT NEED

We recognize appellant's argument (Brief, page 9), "the art of record demonstrate a long-felt need ... for a way to make teratogenic drugs safer." For the reasons set forth above, in our opinion, the long-felt need was recognized and satisfied by another before the date of appellant's invention. Newell Companies v. Kenney Mfg. Co., 864 F.2d 757, 768, 9 USPQ2d 1417, 1426 (Fed. Cir. 1988) (Although at one time there was a long-felt need for a "do-it-yourself" window shade material which was adjustable without the use of tools, a prior art product fulfilled the need by using a scored plastic which could be torn. "[O]nce another supplied the key element, there was no long-felt need or, indeed, a problem to be solved").

According to appellant's evidence (Brief, Appendix I), Woodcock, states "further steps are necessary in addition to the warnings already in place by the manufacturer and the FDA to ensure the safe use of this drug." On this record, Abrams discloses a combination isotretinoin – contraceptive composition. Further, Elsayed discloses the need to provide educational materials to both the consumer and distributor, as well as, providing isotretinoin together with a contraceptive device or formulation. The PDR also demonstrates that the labeling instructions inform consumers to avoid pregnancy during isotretinoin use, and goes as far as recommending that two reliable forms of contraception be used simultaneously unless abstinence is the chosen method.

For these reasons, it is our opinion that the combination of prior art relied upon satisfies the long-felt need prior to the date of appellant's invention.

TIME PERIOD FOR RESPONSE

This opinion contains a new ground of rejection pursuant to 37 CFR § 1.196(b) (2000). 37 CFR § 1.196(b) provides that, “[a] new ground of rejection shall not be considered final for purposes of judicial review.”

37 CFR § 1.196(b) also provides that the appellants, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (§ 1.197(c)) as to the rejected claims:

- (1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner....
- (2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record....

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

VACATED: 37 CFR § 1.196(b)

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Administrative Patent Judge)	
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