

*THIS OPINION WAS NOT WRITTEN FOR PUBLICATION*

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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*Ex parte* MARCHI EGIDIO, ROTINI L. GABRIELE, DESAI SUBHASH and GRILLI MASSIMO

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Appeal No. 1996-0944  
Application No. 08/181,259<sup>1</sup>

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HEARD: October 6, 1999

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Before JOHN D. SMITH, WALTZ, and SPIEGEL, *Administrative Patent Judges*.  
SPIEGEL, *Administrative Patent Judge*.

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<sup>1</sup> Application for patent filed January 13, 1994. According to appellants, this application is a divisional of Application 07/899,421, filed June 16, 1992, now U.S. Patent No. 5,314,904, which issued May 24, 1994.



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Marchi et al. (Marchi) 4,341,785 Jul. 27, 1982

Swedberg et al. (Exhibit A), "Comparison of Single-Dose vs One-Week Course of Metronidazole for Symptomatic Bacterial Vaginosis," 254 *Journal of the American Medical Association* 8, 1046-1049 (Aug. 23/30, 1985).

J. McCue (Exhibit B), "Evaluation and Management of Vaginitis: An Update for Primary Care Practitioners," 149 *Archives of Internal Medicine*, 565-568 (March 1989).

Durfee et al. (Exhibit C), "Ineffectiveness of Erythromycin for Treatment of *Haemophilus vaginalis*-Associated Vaginitis: Possible Relationship to Acidity of Vaginal Secretions," 16 *Antimicrobial Agents and Chemotherapy* 5, 635-637 (November 1979).

B. Majeroni (Exhibit D), "New Concepts in Bacterial Vaginosis," 44 *AFP* 4, 1215-1218 (October 1991).

*Physicians' Desk Reference* (Exhibit E), 47th ed., pages 927-928:METROGEL-VAGINAL (1993).

Treherne et al. (Exhibit F), "In Vitro Studies of *Chlamydia trachomatis* Susceptibility and Resistance to Rifampin and Rifabutin," 33 *Antimicrobial Agents and Chemotherapy* 8, 1393-1394 (August 1989).

*Martindale The Extra Pharmacopoeia*, Thirteenth Edition, page 200:Rifaximin (1993).

The references relied upon by this Merits Panel are:

|                                    |           |                                       |
|------------------------------------|-----------|---------------------------------------|
| Curtis-Prior et al. (Curtis-Prior) | 4,804,674 | Feb. 14, 1989                         |
| Egidio et al. (Egidio)             | 5,314,904 | May 24, 1994<br>(filed Jun. 16, 1992) |

#### ISSUES

Claims 24-30 stand rejected under 35 U.S.C. § 103 as being unpatentable over Parenti in view of Merck and Remington. We **reverse**.

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Pursuant to the provisions of 37 C.F.R. § 1.196(b), we make the following new rejections:

Claim 24 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,314,904. Claim 30 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,314,904 in view of Curtis-Prior. Claims 25-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,314,904 in view of Parenti, Remington and Curtis-Prior.<sup>5</sup>

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims, to the applied prior art references and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's answer (Paper No. 14, mailed September 21, 1995) for the examiner's reasoning in support of the rejection, and to the appellants' brief (Paper No. 12, filed June 30, 1995) and to the appellants' reply brief (Paper No. 14, filed October 6, 1995) for the appellants' arguments thereagainst.

#### *THE INVENTION*

Appellants' invention is directed to a pharmaceutical foam or cream composition for topical treatment of bacterial vaginosis, caused by at least one of *Gardnerella vaginalis*, *Bacteroides bivius*-

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<sup>5</sup>We note that no restriction requirement between method claims and composition claims was made in the record of parent Application 07/899,421. Thus, appellants apparently cancelled the composition claims in '421 voluntarily.

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*disiens*, the species *Mobiluncus* and *Lactobacillus*, *Neisseria gonorrhoeae*, *Haemophilus ducreyi*, and *Chlamydia trachomatis*, wherein the antibacterial agent Rifaximin is the active ingredient in a vaginal compatible carrier (claim 24).

### OPINION

#### ***1. Rejection under 35 U.S.C. § 103***

To establish a *prima facie* case of obviousness, there must be both some suggestion or motivation to modify the reference or combine reference teachings and a reasonable expectation of success. Furthermore, the prior art must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

Parenti discloses that vaginal infections may be caused by yeasts (e.g., *Candida albicans*), protozoans (e.g., *Trichomonas vaginalis*) and/or bacteria (e.g., *Bacteroides spp.* and especially *Gardnerella vaginalis*) (col. 1, lines 22-50). Parenti describes a pharmaceutical composition for topical treatment of infectious vaginitis wherein the antimicrobial purpurmycin is the active ingredient because purpurmycin is effective against all three types of microorganisms, i.e., *Trichomonas*, *Candida* and *Gardnerella* (col. 2, lines 16-32). The topical composition may be provided as a cream

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or foam (col. 5, lines 48-52) in suitable dosage preparations as found in Remington's Pharmaceutical Sciences, 17th Edition, 1985 (col. 5, line 67 - col. 6, line 2).

Merck describes Rifaximin as a nonabsorbable antibacterial agent useful as an intestinal disinfectant, in infectious diarrhea, in hepatic encephalopathy and in intestinal infections.

Remington describes typical foam system topical pharmaceutical formulations.

According to the examiner, since Parenti uses an "antibacterial" agent in a vaginal composition, it would have been obvious to modify the topical, vaginal antibacterial composition of Parenti by using rifaximin as the active ingredient because Merck discloses that rifaximin is an antibacterial agent (answer, pages 3-4). According to the examiner, both the target microorganisms and the target body area(s) treated by the antibacterial composition are "irrelevant" (answer, page 5), i.e., since "rifaximin is known as a pharmaceutical ... it would be obvious to place it in a pharmaceutical composition" (answer, page 4). We disagree.

First, the examiner's proposed modification of Parenti would destroy a fundamental characteristic of Parenti, i.e., the ability to effectively treat each of the three types of infectious vaginitis simultaneously. The examiner has failed to explain what would have motivated one of ordinary skill in the art to destroy such a fundamental characteristic of Parenti.

Second, both the target microorganisms and the target body area(s) are relevant. A target microorganism's sensitivity to a particular antibacterial agent is a primary motivating factor in selecting

that particular antibacterial agent. Here, purpurmycin and rifaximin are structurally unrelated. The examiner has failed to establish why one of ordinary skill in the art would have reasonably expected purpurmycin and rifaximin to be effective against at least one common microorganism. Neither Parenti nor Merck disclose or suggest that rifaximin is effective against *Gardnerella vaginalis*, *Bacteroides bivius-disiens*, the species *Mobiluncus* and *Lactobacillus*, *Neisseria gonorrhoeae*, *Haemophilus ducreyi* or *Chlamydia trachomatis*. The only place we find such a teaching is in appellants' specification. Furthermore, the particular target body area(s) is relevant both to the type of microorganisms expected to be found there and to the pharmacokinetics of the active agent, e.g., delivery means, stability, clearance rate, etc. As noted by appellants, the prior art discloses using rifaximin to treat intestinal infections caused by totally unrelated bacteria, e.g., *Escherichia coli*, *Salmonella*, *Enterococcus*, etc. (brief, pages 10-11, 16). Thus, while the examiner is correct that only a reasonable expectation of success, not absolute predictability, is required to establish a *prima facie* case of obviousness, the examiner has failed to establish the requisite reasonable expectation of success on this record. Moreover, the examiner has not rebutted appellants' arguments that whether a known antibiotic will be effective against bacterial vaginitis is unpredictable, even with related antibiotics such as rifampin and rifabutin, (see e.g., Exhibits C and F) and that effective antibiotics may be contraindicated because of the target body area (see e.g., Exhibits D and E) (brief, pages 12-14 and reply brief, page 2).

A discussion of Remington is not necessary to our decision since Remington does not remedy the deficiencies noted above.

We find that the examiner has relied on impermissible hindsight in making the determination of obviousness. *In re Fritch*, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) (“It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant’s structure as a template and selecting elements from references to fill the gaps.”). Therefore, the rejection of claims 24-30 under 35 U.S.C. § 103 as being unpatentable over Parenti in view of Merck and Remington is reversed.

**2. New grounds of rejection - 37 C.F.R. § 1.196(b)**

We reject (a) claim 24, (b) claim 30 and (c) claims 25-29 under the judicially created doctrine of obviousness-type double patenting over claims 1-7 of Egidio taken (a) alone, (b) in view of Curtis-Prior and (c) in view of Parenti, Remington and Curtis-Prior.

Claims 1-7 of Egidio read as follows:

1. A method of treatment of a vaginal infection which consists of administering topically to a subject in need of treatment a vaginal pharmaceutical composition containing a therapeutically effective amount of Rifaximin in the form of a foam, a cream, a gel, a vaginal ovule or a vaginal capsule.

2. The method according to claim 1 wherein said treatment is with said foam, the flora of *Gardnerella vaginalis*, *Mobiluncus* spp., *Bacteroides* spp. and *Streptococcus pyogenes* are eliminated and the vaginal bacterial flora is normalized with the reappearance of the *Doderlein’s bacillus*.

3. The method according to claim 1 wherein said vaginal infection consists of bacterial vaginosis.

4. The method of treatment of a vaginal infection according to claim 1 which consists of applying by the topical route a pharmaceutically effective amount of Rifaximin to a patient in need of said treatment.

5. The method according to claim 4 wherein said vaginal infection consists of bacterial vaginosis.

6. The method according to claim 4 wherein said topical application is carried out by means of a vaginal foam.

7. The method according to claim 4 wherein said topical application is carried out by means of a cream.

Thus, the claimed pharmaceutical composition is obvious over the pharmaceutical composition specifically required by the methods of Egidio.

Appealed claim 24 requires between 50 and 500 mg of rifaximin while claim 1 of Egidio recites a “therapeutically effective amount” of rifaximin. In order to determine what constitutes a “therapeutically effective amount” of rifaximin, one must consult the specification of Egidio. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970) (the specification of a patent may be consulted under these circumstances not as prior art, but “to learn the meaning of terms in a claim”). Turning to Egidio, col. 2, lines 24-26, we find that as in the present invention a “therapeutically effective amount of rifaximin, [is] preferably between 50 mg and 500 mg.” Thus, it is apparent that claims 1-7 of Egidio encompass the pharmaceutical composition of appealed claim 24.

Appealed claim 30 requires a vaginal cream composition wherein the vaginal compatible carrier is white vaseline, liquid paraffin, white wax, hydrogenated castor oil or methyl glucose dioleate. Curtiss-Prior discloses usual excipients, e.g., carriers, for vaginal creams to include a hydrocarbon base, e.g., white petroleum (i.e., white vaseline) and emulsifiers (col. 2, lines 14-17 and 35-39). Therefore, it would have been obvious to use a conventional excipient such as white vaseline as a carrier in the claimed vaginal cream as disclosed and suggested by Curtis-Prior.

Appealed claims 25-29 requires a vaginal foam composition having micronized rifaximin particles in a vaginal compatible carrier including a thickening agent (i.e., emulsifier) and an oily substance, wherein the foam is contained in an aluminum canister coated internally with an epoxyphenolic resin, closed with a polyethylene valve and having a propellant gas. However, Parenti, Remington and Curtiss-Prior suggest these added limitations as conventional in the art of foam aerosol pharmaceutical compositions. Curtiss-Prior discloses vaginal foams containing a fluorinated hydrocarbon propellant and a surfactant or emulsifier, as well as cetyl alcohol, stearyl alcohol and sodium lauryl sulphate as emulsifiers (col. 2, lines 35-46). Remington discloses foam systems using a blend of propane/isobutane or a hydrocarbon propellant (para. bridging pages 1697-98; page 1700, col. 2, para. 1; page 1701, last para. - page 1702, col. 1, first 5 paras.); aluminum containers lined with epoxy, vinyl or phenolic resins (page 1703, col. 2, first full para.; page 1707, col. 2, first full para.); valves which may have dip tubes of polyethylene (page 1704, col. 2); use of lubricants, e.g., mineral oil,

to prevent agglomeration and lubricate parts of the valve (page 1706, col. 2, penultimate para.); supplying antibacterial agents as dispersions or suspension, i.e., particulate aerosols (page 1706, col. 2, para. 4); and, emulsifiers, including glycols and glycol derivatives (page 1707, col. 1, para. 5). Parenti discloses the conventionality of micronized particulate antibacterial agents in pharmaceuticals (col. 6, lines 3-10). Therefore, it would have been both obvious and within the ordinary skill in the art to provide a vaginal foam composition in a conventional aluminum container lined with a conventional epoxy/phenolic resin and having a conventional (fluorinated) hydrocarbon propellant to provide a conventionally presented particulate (i.e., micronized) antibacterial agent in a conventional carrier comprising emulsifiers and lubricants as suggested by Parenti, Remington and Curtis-Prior. Selection of component amounts and particle sizes would have been a matter of routine optimization within the ordinary skill in the art.

#### *CONCLUSION*

To summarize, the decision of the examiner to reject claims 24-30 under 35 U.S.C. § 103 as unpatentable over Parenti in view of Merck and Remington is **reversed**. However, (a) claim 24, (b) claim 30 and (c) claims 25-29 are rejected pursuant to the provisions of 37 C.F.R.

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§ 1.196(b) under the judicially created doctrine of obviousness-type double patenting over claims 1-7 of Egidio taken (a) alone, (b) in view of Curtis-Prior and (c) in view of Parenti, Remington and Curtis-Prior.

This decision contains a new ground of rejection pursuant to 37 C.F.R. § 1.196(b) (amended effective Dec. 1, 1997, by final rule notice, 62 Fed. Reg. 53, 131, 53, 197 (Oct. 10, 1997), 1203 off. Gaz. Pat. & Trademark Office 63, 122 (Oct. 21, 1997)). 37 CFR § 1.196(b) provides that, “a new ground of rejection shall not be considered final for purposes of judicial review.”

37 C.F.R. § 1.196(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the two following 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 ...

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

**REVERSED - 1.196(b)**

|                             |                   |
|-----------------------------|-------------------|
| JOHN D. SMITH               | )                 |
| Administrative Patent Judge | )                 |
|                             | )                 |
|                             | )                 |
|                             | )                 |
|                             | ) BOARD OF PATENT |
| THOMAS A. WALTZ             | ) APPEALS         |
| Administrative Patent Judge | ) AND             |
|                             | ) INTERFERENCES   |
|                             | )                 |
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| CAROL A. SPIEGEL            | )                 |
| Administrative Patent Judge | )                 |

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