

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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

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*Ex parte* KARL KOLTER, ROLAND BODMEIER, and  
ANDRIY DASHEVSKIY

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Appeal 2008-3443  
Application 10/507,607  
Technology Center 1600

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Decided: August 27, 2008

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Before DEMETRA J. MILLS, ERIC GRIMES, and LORA M. GREEN,  
*Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

**DECISION ON APPEAL**

This is an appeal under 35 U.S.C. § 134 involving claims to a controlled release dosage form. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

## BACKGROUND

The Specification states that the

solubility of numerous medicinal substances is pH-dependent, and therefore conventional slow-release forms show pH-dependent release. . . . Release of active ingredient is usually fastest at the pH at which the solubility of the active ingredient is greatest, because the concentration gradient from the inside to the outside of the film is then greatest. There have been various attempts to solve this problem, but to date they have all been unsatisfactory and, in some cases, have serious disadvantages.

(Spec. 2.)

The Specification discloses that the

[c]ombination of polyvinyl acetate with acid-insoluble or alkali-insoluble polymers allows deliberate adjustment of the permeability properties of the coating, so that a pH-independent release results. For this purpose, in the case of an active ingredient which is more soluble at acidic pH there is use of an acid-insoluble polymer which reduces the permeability of the coating in the acidic range but increases it in the alkaline range, where the solubility of the medicinal substance is low. In the case of active ingredients which are more soluble in the alkaline range, an alkali-insoluble polymer is employed. Solubility of the active ingredient and permeability of the coating must always behave in a contrary way. The ratio of polyvinyl acetate to acid-insoluble or alkali-insoluble polymer depends on the solubility differences of the active ingredient at various pH values, i.e. the greater the difference, the more acid-insoluble or alkali-insoluble polymer must be used.

(*id.* at 5.)

## DISCUSSION

### 1. CLAIMS

Claims 1-11 and 13-19 are on appeal. Claim 12 is allowed (App. Br. 2).

Claims 1 and 9 are representative and read as follows:

Claim 1: An active ingredient-containing dosage form which is provided with a film coating and has controlled, pH-independent release, where the film coating has a thickness of between 20 and 200 µm and comprises

(A) 10-99% by weight of polyvinyl acetate,

(B) 1-50% by weight of at least one polymer selected from the group consisting of lipophilic water-insoluble polymers, acid-insoluble polymers and alkali-insoluble polymers, and

(C) 0-50% by weight of other pharmaceutically acceptable aids, the total of components (A), (B) and (C) is 100% by weight and the ratio of (A) to (B) is from 70:30 to 99:1.

Claim 9: A dosage form as claimed in claim 1, where the polyvinyl acetate has a molecular weight of from 10 000 to 2 000 000.

### 2. OBVIOUSNESS I

Claims 1-8, 10, 11 and 13-18 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Morella<sup>1</sup> and Bartholomaeus.<sup>2</sup>

The Examiner relies on Morella as disclosing “a sustained release composition comprising an active core and a core coating that is partially soluble at a highly acidic pH” (Answer 3). The Examiner further relies on Morella as disclosing that the “core coating comprises at least one enteric polymer in an amount of from about 1% to 60%, at least one insoluble

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<sup>1</sup> Morella et al., US Patent 5,202,128, Apr. 13, 1993.

<sup>2</sup> Bartholomaeus et al., US 6,576,260 B2, Jun. 10, 2003.

matrix polymer in an amount of from about 1% to 85%, and at least one partially acid soluble polymer in an amount of from about 1% to 60%” and that exemplary (insoluble matrix) polymers include “ethyl cellulose, acrylate/methacrylate copolymer, and the like” (*id.* at 4). The Examiner further relies on Morella for disclosing that “the core coating has a thickness of approximately 5  $\mu\text{m}$  to 200  $\mu\text{m}$ ” (*id.*).

The Examiner finds that “Morella does not explicitly teach polyvinyl acetate in the core coating composition” (*id.*). The Examiner relies on Bartholomaeus as disclosing a sustained release coating formulation that can comprise a water-insoluble polymer such as polyvinyl acetate (*id.*).

The Examiner concludes that “it would have been obvious to one of ordinary skill in the art to modify the water insoluble matrix polymer of Morella using polyvinyl acetate in view of the teaching of Bartholomaeus,” because Bartholomaeus teaches that polyvinyl acetate “can be used to produce the sustained release coating that provides advantageous results for highly water soluble active agent,” and “Morella teaches the desirability of obtaining a sustained release dosage form suitable for highly water-soluble active agent” (*id.* at 4-5).

Appellants argue that the combination of Morella and Bartholomaeus does not suggest a dosage form that is pH-independent, as is required by claim 1 (Appeal Br. 5-12). Appellants argue that the fact that the core dosage forms of Morella “exhibit a pH dependent release of the active ingredient is ...evident from the abstract of the reference” (*id.* at 5).

The Examiner responds that the “present specification does not define the term ‘pH-independent’...[and] the examiner is unable to determine the

intended meaning for the limitation ‘pH-independent’” (Answer 10). The Examiner also argues that the Specification “discloses [that] at acidic pH, the permeability of the coating is reduced but increased in the alkaline pH” (*id.*, citing the Spec. at p. 5, ll. 25-27).

We agree with Appellants that the Examiner has not adequately explained how the references would have suggested a “pH-independent” dosage form having the claimed components.

Morella discloses a “pharmaceutical composition [that] provides a slow release of active ingredient at a highly acidic pH and provides a constant, relatively faster rate of release at a more alkaline pH such as that of the intestine” (Morella, abstract). Morella also discloses that the coating of the disclosed dosage form “may include at least one polymer which is substantially insoluble independent of pH (insoluble matrix polymer); at least one enteric polymer which is substantially insoluble at acidic pH but at least partially soluble at a less acidic to basic pH (enteric polymer); and at least one component which is at least partially soluble at acidic pH (acid soluble polymer)” (*id.* at col. 8, ll. 31-38).

Bartholomaeus discloses “sustained-release formulations of tramadol comprising tramadol saccharinate coated with at least one sustained-release coating” (Bartholomaeus, abstract). Bartholomaeus also discloses that “the sustained-release coating film is preferably based on a water-insoluble, optionally modified, natural and/or synthetic polymer” (*id.* at col. 3, ll. 44-46) and that preferred water-insoluble polymers include polyvinyl acetates (*id.* at col. 4, ll. 1-4). Bartholomaeus also provides a working example in which “the release profile of the tramadol saccharinate pellets provided with

a sustained-release coating” is not affected by the pH of the release medium (*id.* at col. 8, ll. 55-62).

We agree with Appellants that the Examiner has not adequately shown that the cited references support a *prima facie* case of obviousness. First, the Examiner has not adequately explained why a person of ordinary skill in the art would have been led to combine a component of Bartholomaeus’ pH-independent dosage form with Morella’s dosage form, which is expressly designed to provide pH-dependent release.

In addition, the Examiner has not adequately explained how modification of the pH-dependent dosage form of Morella to contain polyvinyl acetate as the insoluble polymer would have achieved the claimed pH-independent dosage form. That is, even if the polyvinyl acetate disclosed by Bartholomaeus were used as the insoluble matrix polymer in Morella’s dosage form, the Examiner has not provided an adequate basis to conclude that the resulting dosage form would provide “controlled, pH-independent release,” as recited in the instant claims.

In response to Appellants’ argument on this point, the Examiner stated that the “specification does not define the term ‘pH-independent’... [and] the examiner is unable to determine the intended meaning for the limitation ‘pH-independent’” (Answer 10). As we understand it, the Examiner’s position is that “pH-independent release” does not limit the claims because the phrase is not precisely defined.

We do not agree with this position. The Specification makes clear that “pH-independent release” is determined in reference to the dosage form

as a whole and not specifically the coating on the dosage form. For example, the Specification states:

Combination of polyvinyl acetate with acid-insoluble or alkali-insoluble polymers allows deliberate adjustment of the permeability properties of the coating, so that a pH-independent release results.

...[I]n the case of an active ingredient which is more soluble at acidic pH there is use of an acid-insoluble polymer which reduces the permeability of the coating in the acidic range but increases it in the alkaline range, where the solubility of the medicinal substance is low. In the case of active ingredients which are more soluble in the alkaline range, an alkali-insoluble polymer is employed. Solubility of the active ingredient and permeability of the coating must always behave in a contrary way. The ratio of polyvinyl acetate to acid-insoluble or alkali-insoluble polymer depends on the solubility differences of the active ingredient at various pH values, i.e. the greater the difference, the more acid-insoluble or alkali-insoluble polymer must be used.

(Spec., p. 5, ll. 21-26.)

Therefore, because the Examiner has not adequately explained how the combination of references would have suggested a dosage form which is “pH-independent,” as claimed, the rejection of claims 1-8, 10, 11, and 13-18 as obvious in view of Morella and Bartholomaeus is reversed.

### 3. OBVIOUSNESS II

Claims 9 and 19 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Morella, Bartholomaeus, and Feltz.<sup>3</sup>

The Examiner relies on Morella and Bartholomaeus as discussed above and relies on Feltz as disclosing “a gastrointestinal protective coating formulation comprising polymeric film coating, including[ ] polyvinyl acetate having molecular weight of 12,000 to 167,000” (Answer 5). The

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<sup>3</sup> Feltz et al., US 4,871,546, Oct. 3, 1989.

Examiner concludes that “it would have been obvious to one of ordinary skill in the art to use the polyvinyl acetate having molecular weight of 12,000 to 167,000 in view of Feltz, because Feltz teaches the use of polyvinyl acetate having the claimed molecular weight that is useful as a coating polymer” (*id.*).

We will reverse this rejection. The Examiner has pointed to nothing in Feltz that makes up for the deficiency in Morella and Bartholomaeus. Therefore, the rejection of claims 9 and 19 is obvious in view of Morella, Bartholomaeus, and Feltz is reversed.

#### SUMMARY

We agree with Appellants that the Examiner has not established a *prima facie* case of obviousness based on the evidence of record. We therefore reverse the rejection of claims 1-11 and 13-19 under 35 U.S.C. § 103(a).

#### REVERSED

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