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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* GAIL K. BUEHLER<sup>1</sup>

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Appeal 2015-000755  
Application 12/782,269  
Technology Center 1600

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Before DONALD E. ADAMS, LORA M. GREEN, and RYAN H. FLAX,  
*Administrative Patent Judges.*

FLAX, *Administrative Patent Judge.*

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134(a) involving claims directed to a dye-free pharmaceutical suspension. Claims 1, 4, 6, 7, 9, 12, 14–18, 24, 26, 29, 36, and 37 are on appeal as rejected under 35 U.S.C. § 103(a). We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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<sup>1</sup> We understand the Real Party in Interest to be McNeil-PPC, Inc., a wholly owned subsidiary of Johnson & Johnson. Br. 1.

## STATEMENT OF THE CASE

The appealed claims can be found in the Claims Appendix of the Appeal Brief. Claims 1, 18, and 36 are the independent claims. Claim 1 is representative, and reads as follows:

1. A dye-free pharmaceutical suspension, comprising:

(a) a therapeutically effective amount of a first active agent consisting essentially of a first substantially water insoluble active agent having an average particle size of between about 10 and about 100 microns,

(b) an effective amount of a non-reducing sweetener comprising sorbitol;

(c) an effective amount of water; and

(d) an effective amount of a suspending system;

wherein the dye-free pharmaceutical suspension has a pH of from about 5 to about 6 and is substantially free of a reducing sugar.

Br. 10 (Claims App'x).

The following rejections are on appeal:

Claims 1, 4, 6, 7, 9, 12, 14–18, 24, 26, and 29 stand rejected under 35 U.S.C. § 103(a) over Blase<sup>2</sup> and Kumar.<sup>3</sup> Final Action 3.

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<sup>2</sup> U.S. Patent No. 5,409,907 (issued to Blase on Apr. 25, 1995) (hereinafter “Blase”).

<sup>3</sup> Ashir Kumar, MD, et al., *The Mystery Ingredients: Sweeteners, Flavorings, Dyes, and Preservatives in Analgesic/ Antipyretic, Antihistamine/Decongestant, Cough and Cold, Antidiarrheal, and Liquid Theophylline Preparations*, 91 PEDIATRICS 927–33 (1993) (hereinafter “Kumar”).

Claims 1, 4, 6, 7, 9, 12, 14–18, 24, 26, 29, and 36 stand rejected under 35 U.S.C. § 103(a) over Blase, Kumar, Munshi,<sup>4</sup> and Singh.<sup>5</sup> Final Action 6.

Claims 1, 4, 6, 7, 9, 12, 14–18, 24, 26, 29, 36, and 37 stand rejected under 35 U.S.C. § 103(a) over Blase, Kumar, Munshi, Singh, and Sorrentino.<sup>6</sup> Final Action 8.

Except where otherwise indicated, we adopt the Examiner’s findings of fact, reasoning on scope and content of the prior art, and conclusions set out in the Final Action and Answer. Any findings of fact set forth below are provided to highlight certain determinations by the Examiner or identify facts established by Appellant.

#### FINDINGS OF FACT

FF1. Blase disclosed:

The present invention provides a pharmaceutical suspension comprising a therapeutic amount of a drug; a suspending system consisting essentially of an effective amount of xanthan gum and microcrystalline cellulose to form a stable suspension system in an aqueous solution; water; and optionally an effective amount of sweetening agents and flavoring agents to provide a palatable taste to said pharmaceutical suspension.

Blase col. 2:12–19 (makes no mention of requiring any or a specific sweetener, i.e., “optionally,” and makes no mention of including a dye); *see also* Final Action 3–6 (discussing Blase).

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<sup>4</sup> U.S. Patent No. 4,427,681 (issued to Munshi on Jan. 24, 1984) (hereinafter “Munshi”).

<sup>5</sup> U.S. Patent No. 5,759,579 (issued to Singh et al. on June 2, 1998) (hereinafter “Singh”).

<sup>6</sup> U.S. Patent No. 4,892,877 (issued to Sorrentino on Jan. 9, 1990) (hereinafter “Sorrentino”).

FF2. Blase also disclosed, “[c]oloring agents also may be incorporated in the suspension to provide an appealing color to the suspension.” Blase 6:5–6; *see also* Final Action 3–6 (discussing Blase).

FF3. Blase disclosed, “[t]he flavoring and coloring ingredients added to the mixture should be of the type and amount desired for the particular suspension to meet the preferences dictated by the intended consumer of such suspension e.g. pediatric or adult.” Blase 8:9–13; *see also* Final Action 3–6 (discussing Blase).

FF4. Blase disclosed, “[u]p to about 20 grams pharmaceutical active per 100 mL may be readily taste masked with the addition of sweeteners and flavoring agents. However, this may vary depending on the palatability of the pharmaceutical active.” Blase 4:27–31; *see also* Final Action 3–6 (discussing Blase).

FF5. Blase disclosed, “[m]asking the flavor of bitter pharmaceuticals may be accomplished by using flavoring agents and sweeteners to overpower the bitter flavor of the pharmaceutical. The bitter flavor also can be minimized by limiting the amount of water present in the suspension.” Blase 4:34–38; *see also* Final Action 3–6 (discussing Blase).

FF6. Blase disclosed a substantial selection of sweeteners, including sorbitol and artificial sweeteners, as follows:

Suitable sweetening agents include but are not limited to sugars such as monosaccharides, disaccharides and polysaccharides. Examples of suitable sugars include but are not limited to xylose, ribose, glucose, mannose, galactose, fructose, dextrose, sucrose, maltose, partially hydrolyzed starch or corn syrup, and sugar alcohols such as sorbitol, xylitol, mannitol, glycerin and

combination thereof. Presently preferred as a sugar sweetener is high fructose corn syrup provided as an aqueous solution. . . .

Water soluble artificial sweeteners also may be employed in place of or in addition to sugar sweeteners. Examples of suitable artificial sweeteners include but are not limited to aspartame, sucrose, cyclamates, saccharin and mixtures thereof.

Blase 4:38–60; *see also* Final Action 3–6 (discussing Blase).

FF7. Blase disclosed, “[t]he preferred sweeteners for acetaminophen suspension are high fructose corn syrup, sorbitol and glycerin.” Blase 6:62–63; *see also* Final Action 3–6 (discussing Blase).

FF8. Blase disclosed how and in what amount to include fructose, sorbitol, or glycerin as the sweetener:

The high fructose corn syrup should be provided as an aqueous solution containing 77% by weight solid. The fructose content of the high fructose corn syrup should be about 55%. The amount of aqueous high fructose corn syrup percent in the acetaminophen suspension should be in the range of from about 20 to about 80 grams per 100 ml of suspension. The sorbitol also should be present as an aqueous solution containing 70% sorbitol by weight. The amount of aqueous sorbitol present in the acetaminophen suspension should be in the range of from about 1 to about 30 grams of sorbitol per 100 mL of the suspension. The amount of glycerin in the acetaminophen suspension should be in the range of from about 1 to about 20 grams of glycerin per 100 mL of the suspension.

Blase 6:64–7:10; *see also* Final Action 3–6 (discussing Blase).

FF9. Blase claimed its pharmaceutical suspension includes a sweetening agent, as follows:

selected from the group consisting of xylose, ribose, glucose, mannose, galactose, fructose, dextrose, sucrose, maltose, partially hydrolyzed starch solids, partially hydrolyzed corn

syrup solids, sorbitol, xylitol, mannitol, glycerin, aspartame, sucralose, cyclamates, saccharin and mixtures thereof.

Blase claim 2; *see also* Final Action 3–6 (discussing Blase).

FF10. Kumar disclosed, “[a]dverse effects reported with sweeteners are summarized in Table 10. . . . [S]ome of these adverse effects (eg, cariogenicity, osmotic diarrhea) are dose related . . . .” Kumar 928 (right col.); *see also* Br. 7 (contending Kumar teaches away from sorbitol as excipient); *cf.* Ans. 10–11 (contending Kumar explains any adverse effects of sorbitol are dose dependent and arguing a lack of evidence on dose and other prior art).

FF11. Kumar disclosed sorbitol can cause the following adverse effects: “[o]smotic diarrhea, poor absorption of active drug, flatulence, [and] abdominal pain.” Kumar 932 (table 10); *see also* Br. 7 (contending Kumar teaches away from sorbitol as an excipient).

FF12. Munshi disclosed, “[c]ompositions employing titanium dioxide as an opacifying agent and which are thixotropic gels easily convertible to pourable liquids with moderate shaking” and “the product is converted to a pourable liquid having a viscosity of from about 300 to about 800 cps.” Munshi Abstract and col. 2:1–4; *cf.* Br. 7–8 (contending Munshi’s disclosed gels are not liquid suspensions); *see also* Spec. 2:14–18 (distinguishing suspensions from emulsions).

FF13. Munshi disclosed, “the compositions of this invention can contain any suitable optional ingredients such as buffers, flavorants, colorants, sweeteners, preservatives, solubilizing agents and the like in amounts generally known for these agents.” Munshi 3:26–

30; *see also* Final Action 7 and Ans. 11 (identifying that colorants are optional in Munshi).

## DISCUSSION

We discuss all obviousness rejections together because they were argued together by Appellant. We conclude the Examiner has established a *prima facie* case that the claims would have been obvious over the cited prior art combinations. We address Appellant's arguments below.

Appellant argues, "Blase [] does not disclose or suggest a dye-free suspension composition that is substantially free of a reducing sugar. In fact, Blase [] does not even mention or discuss reducing sugars," and "[i]t is clear that Blase [] did not contemplate formulating a dye free suspension, nor did Blase [] understand the detrimental effects that reducing sugars have on the stability of dye free suspensions." Br. 6. Regarding the "dye-free" claim element, Appellant contends the Examiner's determination that colorant/dye is merely optional in the Blase and Munshi formulations is incorrect because each example in the references includes colorant. Br. 8. Regarding the "substantially free of a reducing sugar" claim element, Appellant contends the Blase formulations require high fructose corn syrup, which is a reducing sugar (*see* Spec. 7:17–8:2), and argue that one of ordinary skill in the art would not substitute sorbitol or glycerin for such fructose because the solution could never be sweet enough using reasonable amounts of the alternative sweeteners. Br. 7. We are not persuaded by these arguments.

The cited prior art teaches and suggests a dye-free pharmaceutical formulation. Blase, in describing its most basic invention, disclosed a

pharmaceutical suspension with several components, none of which was a dye or coloring. FF1. It is apparent from the remainder of the Blase disclosure that including dye is an option, but it is equally apparent from the full Blase disclosure that it is not required. *See* FF2 and FF3. Whether each example provided by Blase includes dye or coloring is not determinative, because the test of obviousness is “whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention.” *In re Gorman*, 933 F.2d 982, 986 (Fed. Cir. 1991).

Similarly, while each Blase example includes fructose as a sweetener and Blase identifies fructose as its preferred sweetener, the reference’s disclosure is not so limited. Blase discloses many alternatives to fructose, including sorbitol and several artificial sweeteners, and it is unquestionable that the Blase compositions can be free of fructose and free of a reducing sugar. *See* FF6–FF9. Appellant’s arguments regarding the sweetness of fructose and that of other Blase-disclosed sweeteners, and the amounts of each required to provide equivalent sweetness are not persuasive. *See* Br. 6. The appealed claims do not recite any specific, required sweetness factor and Blase expressly discloses suitable amounts of sorbitol or glycerin to be provided in its pharmaceutical solutions. *See* FF8.

Appellant contends Kumar teaches away from using the recited sorbitol because the reference discloses it can cause diarrhea, poor drug absorption, flatulence, and abdominal pain, in a rationale largely paralleling that of the Examiner for omitting dye from the pharmaceutical of Blase and Munshi. Br. 7; *see also* FF10 and FF11 (relevant portions of Kumar). An important difference between the two positions exists, however, in that Blase

suggests either including or not including dye, which makes each alternative obvious, and suggests including sorbitol, which makes using this sweetener obvious. Therefore, although it might be obvious not to include sorbitol because it could present adverse effects, it is also obvious to include it because the Blase reference expressly suggests doing so. The fact that the use of sorbitol might have some drawbacks is not determinative of obviousness, as “a given course of action often has simultaneous advantages and disadvantages, and this does not necessarily obviate motivation to combine” or to modify or select certain embodiments from the prior art. *Medichem, S.A. v. Rolabo S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006).

Finally, Appellant argues Munshi is not relevant because its disclosure is directed to thixotropic gels rather than liquid suspensions. Br. 7–8. This is not persuasive.

While Munshi does disclose that its pharmaceutical compositions are initially thixotropic gels, which may or may not be significantly different from liquid suspensions (this is not entirely clear because the Specification only explicitly distinguishes liquid suspensions from emulsions—*see* Spec. 2:14–18), the reference also discloses that these gels are “easily convertible to pourable liquids,” which may or may not include suitable optional ingredients, such as colorants and sweeteners. FF12 and FF13. Appellant does not address this aspect of Munshi’s disclosure, which refutes her arguments thereover.

For the above reasons, we find the preponderance of evidence supports the Examiner’s determination of obviousness. We affirm the rejections.

SUMMARY

The rejection under 35 U.S.C. § 103(a) over Blase and Kumar is affirmed.

The rejection under 35 U.S.C. § 103(a) over Blase, Kumar, Munshi, and Singh is affirmed.

The rejection under 35 U.S.C. § 103(a) over Blase, Kumar, Munshi, Singh, and Sorrentino is affirmed.

All claims fall with claim 1. 37 C.F.R. § 41.37(c)(1)(iv).

TIME PERIOD FOR RESPONSE

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

AFFIRMED