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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* KARL-JOSEF HUBER-HAAG, MARIE-CLAIRE FICHOT,  
FLORENCE ROCHAT, and NORBERT SPRENGER<sup>1</sup>

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Appeal 2014-005255  
Application 12/593,462  
Technology Center 1600

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Before ERIC B. GRIMES, ULRIKE W. JENKS, and  
RACHEL H. TOWNSEND, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to administering to an infant delivered by caesarean section a probiotic and prebiotic composition for promoting the development of an early bifidogenic intestinal microbiota, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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<sup>1</sup> Appellants identify the Real Party in Interest as Nestec S.A. (Appeal Br. 2.)

## STATEMENT OF THE CASE

During the normal process of vaginal birth, the gastrointestinal tract of a baby encounters bacteria from the digestive tract, skin, and environment of the mother and starts to become colonized, whereas immediately before birth, the gastrointestinal tract is thought to be sterile. (Spec. 1.) It has been determined that “the rates of colonisation by Bifidobacteria . . . in [infants born by] caesarean [section] . . . reached the rates of colonisation in the vaginally delivered group only after one month.” (*Id.*)

“[I]t has recently been demonstrated that human milk contains not only oligosaccharides but also Bifidobacteria.” (Spec. 3.) “Mother’s milk is recommended for all infants. However, in some cases breast feeding is inadequate or unsuccessful for medical reasons or the mother chooses not to breast feed.” (Spec. 2.)

“[M]ore and more evidence is emerging which suggests that the establishment of an appropriate intestinal microbiota early in life may be . . . significant in subsequent healthy development.” (Spec. 3.) Appellants’ invention is directed to promoting the “establishment of an appropriate intestinal microbiota in infants where this does not occur naturally.” (*Id.*)

Claims 1, 7–9, and 11–15 are on appeal.<sup>2</sup> Claim 1 is representative and reads as follows:

1. A method for promoting the development of an early bifidogenic intestinal microbiota in infants delivered by caesarean section comprising the step of administering to an infant delivered by caesarean section a composition comprising

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<sup>2</sup> Claims 2, 3, 10, and 16–39 are also pending, but stand withdrawn from consideration. (Ans. 2.)

*Bifidobacterium lactis* CNCM I-3446 and an oligosaccharide mixture which comprises 5–20 wt% of at least one N-acetylated oligosaccharide selected from the group consisting of GalNAc $\alpha$ 1,3Gal $\beta$ 1,4Glc and Gal $\beta$ 1,6GalNAc $\alpha$ 1,3Gal $\beta$ 1,4Glc, 60–90 wt% of at least one neutral oligosaccharide selected from the group consisting of Gal $\beta$ 1,6Gal, Gal $\beta$ 1,6Gal $\beta$ 1,4Glc, Gal $\beta$ 1,6Gal $\beta$ 1,6Glc, Gal $\beta$ 1,3Gal $\beta$ 1,3Glc, Gal $\beta$ 1,3Gal $\beta$ 1,4Glc, Gal $\beta$ 1,6Gal $\beta$ 1,6Gal $\beta$ 1,4Glc, Gal $\beta$ 1,6Gal $\beta$ 1,3Gal $\beta$ 1,4Glc, Gal $\beta$ 1,3Gal $\beta$ 1,6Gal $\beta$ 1,4Glc and Gal $\beta$ 1,3Gal $\beta$ 1,3Gal $\beta$ 1,4Glc and 5–30 wt% of at least one sialylated oligosaccharide selected from the group consisting of NeuAc $\alpha$ 2,3Gal $\beta$ 1,4Glc and NeuAc $\alpha$ 2,6Gal $\beta$ 1,4Glc.

(Appeal Br. 13.)

The following ground of rejection by the Examiner is before us on review<sup>3</sup>:

Claims 1, 7–9, and 11–15 under 35 U.S.C. § 103(a) as unpatentable over Boehm<sup>4</sup>, Donnet-Hughes,<sup>5</sup> Sprenger,<sup>6</sup> Isolauri,<sup>7</sup> and Masco.<sup>8</sup>

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<sup>3</sup> The provisional obviousness-type double patenting rejections that were pending as of the Final Office Action have been withdrawn in light of the abandonment of the copending applications over which the rejections were made. (Ans. 3.)

<sup>4</sup> Boehm et al., WO 2007/045502 A1, published Apr. 26, 2007, and filed Oct. 20, 2006.

<sup>5</sup> Donnet-Hughes et al., WO 2006/108824 A1, published Oct. 19, 2006.

<sup>6</sup> Sprenger et al., WO 2007/101675 A1, published Sept. 13, 2007, and filed Mar. 7, 2007.

<sup>7</sup> E. Isolauri et al., *Probiotics: a role in the treatment of intestinal infection and inflammation?* 50 (Suppl. III) *Gut*, iii54–iii59 (2002).

<sup>8</sup> Liesbeth Masco et al., *Polyphasic taxonomic analysis of *Bifidobacterium animalis* and *Bifidobacterium lactis* reveals relatedness at the subspecies level: reclassification of *Bifidobacterium animalis* as *Bifidobacterium animalis* subsp. *animalis* subsp. nov. and *Bifidobacterium lactis* as*

## DISCUSSION

The Examiner finds that Boehm teaches infants delivered by caesarean section have a different intestinal flora compared with infants born vaginally. (Ans. 5.) Boehm also teaches that a healthy intestinal flora reduces incidence of infections and provides for a strengthened immune system and it is of “utmost importance to stimulate the healthy development of the intestinal flora of infants born via cesarean section.” (Final Action 3–4; Ans. 5.) According to the Examiner, Boehm teaches that breast milk is “the gold standard” for developing nutrition for infants in order “to mimic the compositional features and physiological effects of human breast milk” and that human breast milk contains prebiotic fiber that stimulates the development of a healthy intestinal flora. (*Id.*) The Examiner finds that Boehm teaches a method for stimulating the development of a healthy intestinal flora in an infant delivered by c-section comprising administering a composition that includes at least one microorganism that may be *Bifidobacterium bifidum* (now known as *Bifidobacterium lactis* (as indicated by Isolauri), which is a subspecies of *Bifidobacterium animalis* (as indicated by Masco)) and at least one indigestible oligosaccharide. (Final Action 4–5; Ans. 5–6.) The indigestible oligosaccharide benefits the host “by selectively stimulating the growth and/or activity of one or a limited number of bacterial species in the colon.” (*Id.*) Boehm also teaches that “the composition can be admixed with breast milk[,] which will contain additional oligosaccharides.” (*Id.*) The Examiner acknowledges that Boehm does not

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*Bifidobacterium animalis subsp. lactis subsp. nov.*, 54 Int. J. Syst. Evol. Microbiol., 1137–43 (2004).

teach the specifically claimed strain of *B. lactis* or the specific oligosaccharide mixture claimed. (Final Action 6; Ans. 7.) However, the Examiner finds that Donnet-Hughes and Sprenger suggest these specific elements in a nutritional formula for infants.

In particular, the Examiner finds that, like Boehm, Donnet-Hughes is concerned with promoting the development of a beneficial intestinal microbiota in infants. (Ans. 9; Final Action 6.) Where Boehm is concerned specifically with infants delivered by c-section, Donnet-Hughes is concerned with neonates generally, which the Examiner notes includes infants delivered via c-section. (Ans. 7.) In Donnet-Hughes, the neonate is provided with a probiotic bacteria, such as *B. lactis* CNCM I-3446, and the formulation provided to the neonate can also include carbohydrates and fibers. (Final Action 6; Ans. 7.) Moreover, the Examiner finds that Donnet-Hughes teaches that adding the foregoing to the neonate diet stimulates beneficial intestinal microbiota, and promotes the maturation of the immune system of the neonatal infant, just as Boehm teaches is the case with c-section babies provided with probiotic Bifidobacterium and a prebiotic combination. (Ans. 8–9; Final Action 6.) The Examiner finds that Sprenger teaches an infant formula composition that comprises probiotic bacteria and the prebiotic oligosaccharides recited in claim 1. (Final Action 6; Ans. 7.)

According to the Examiner, the foregoing facts would have suggested to the person of ordinary skill in the art to substitute *B. lactis* CNCM I-3446 in the Boehm formulation for the “predictable result of successfully stimulating the development of a healthy intestinal flora in an infant (delivered by caesarean section).” (Ans. 8–9; Final Action 7.) The

Examiner further finds that one of ordinary skill in the art would have further been motivated to include the oligosaccharide mixture of Sprenger so that the infant formula composition would more closely resemble breast milk and stimulate the healthy development of the intestinal flora of infants. (Ans. 7–9; Final Action 8–9.)

We agree with the Examiner’s factual findings and conclusion that Boehm, Donnet-Hughes, and Sprenger make obvious the claimed method of promoting the development of an early bifidogenic intestinal microbiota in infants delivered by c-section using the recited composition.

Appellants argue that the references fail to suggest administering to an infant delivered by c-section the specifically claimed *B. lactis* strain (Appeal Br. 6–8). In particular, Appellants contend that “the teachings of *Donnet-Hughes* regarding neonatal infants generally are not necessarily applicable to infants born by caesarean delivery” because “[t]he overall pattern of combination of risks in infants born by caesarean delivery is fundamentally different from the risk of the general infant population” and “*Donnet-Hughes* is entirely directed to development of intestinal microbiota in formula-fed infants in order to more closely conform the intestinal microbiota to that of breast fed babies” and is “completely silent regarding infants born by caesarean delivery.” (Appeal Br. 7.) Further, according to Appellants, “*Boehm* itself demonstrates that the teachings of *Donnet-Hughes* regarding neonatal infants generally are not necessarily applicable to infants born by caesarean delivery by disclosing that, for infants delivered by caesarean section, ‘their intestinal flora at birth is completely different from the intestinal [flora of] infants born via the vaginal route.’” (Appeal Br. 7–

8.) Appellants further contend that prior art demonstrates that health benefits conferred by a specific bacterial strain to a host are strain specific and are not predictable. (Appeal Br. 7 (citing Senok<sup>9</sup>); Reply Br. 3–4.) We do not find these arguments persuasive.

In particular, whether the overall risk pattern may be different between infants delivered via c-section and infants generally, Donnet-Hughes is concerned with neonates as a class; as the Examiner noted (Ans. 11), the neonate class of Donnet-Hughes does not exclude infants delivered by c-section. Moreover, whether Donnet-Hughes is concerned with mimicking the intestinal microbiota of breast fed babies, it, nevertheless, teaches the use of *B. lactis* CNCM I-3446 for the purpose of promoting the development of a beneficial intestinal microbiota and to promote the maturation of the immune system of a neonatal infant “in need thereof.” (Donnet-Hughes 3 and Abstr.) Donnet-Hughes explains that in some situations infants are not breast fed for a variety of reasons, and regardless of reason, the gut microbiota of non-breast fed infants is different from that of breast fed infants including with respect to the population of Bifidobacteria. (Donnet-Hughes 1.) Similar to the difference in gut bacteria noted by Donnet-Hughes, Boehm teaches that infants delivered by c-section lack several species of Bifidobacteria, as compared to those born vaginally, including *B. lactis*. (Boehm 14–16 (Tables 1 and 2).) Boehm further teaches that “biodiversity [of the intestinal flora] is of great importance for achieving the desired physiological effects and optimally stimulate the

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<sup>9</sup> A. C. Senok et al., *Probiotics: facts and myths*, 11(12) Clin. Microbial. Infect., 958–66 (2005).

health of the infant” and thus indicates that, among other probiotics, *B. lactis* would be a beneficial probiotic to administer to infants (Boehm 2–4, 18 (Example 4), 7.) Consequently, Boehm teaches that infants born via c-section would be “in need” of promoting maturation of the immune system just like neonates who are not breast fed and that *B. lactis* would be one of the beneficial species to provide.

Appellants’ argument that Donnet-Hughes “fails to suggest that *B. lactis* CNCM I-3446 can be used to treat any of the specific health conditions of the caesarean-section infants that the claimed invention targets and solves” (Appeal Br. 7; Reply Br. 2) is also unavailing.

In determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls. . . . [A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.

*KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 419–20 (2007). As discussed, Donnet-Hughes teaches that *B. lactis* CNCM I-3446 promotes the development of a beneficial intestinal microbiota and the maturation of the immune system of a neonatal infant “in need thereof,” such as those that are not breast fed and thus have a less appreciable population of Bifidobacteria than those that are breast fed. (Donnet-Hughes 1.) And Boehm teaches that infants delivered via c-section, like those who are not breast fed, have a less appreciable population of Bifidobacteria than infants who are born vaginally. Thus, regardless of the fact that Donnet-Hughes may not identify that *B. lactis* CNCM I-3446 “can be used to treat any of the specific health conditions of the caesarean-section infants that the claimed invention targets

and solves” (Appeal Br. 7; Reply Br. 2) it, nevertheless, provides incentive for one of ordinary skill in the art to select that strain of *B. lactis* to use in the Boehm method of increasing the species of beneficial intestinal flora in infants delivered by c-section.

We disagree with Appellants that Boehm or Senok support finding it unpredictable as to whether c-section infants would similarly benefit if the *B. lactis* provided was *B. lactis* CNCM I-3446. That the intestinal flora is different between infants delivered vaginally and by c-section does not suggest that addition of *B. lactis* CNCM I-3446 to the diet of these infants would not promote the maturation of the immune system of c-section infants just as Boehm indicates *B. lactis* generally would. Moreover, while Senok indicates generally that “[c]urrent evidence indicates that probiotic effects are strain-specific” (Senok 959), the Examiner has provided prima facie evidence that *B. lactis* CNCM I-3446 administered to infants regardless of the method of delivery of the infant would be expected to promote the maturation of the immune system. As already noted, the neonate population of Donnet-Hughes does not differentiate between infants delivered vaginally or by c-section, noting simply the importance of promoting development of the beneficial intestinal microbiota in neonatal infants and accomplishing this goal with provision of *B. lactis* CNCM I-3446. Sprenger notes, like Boehm, that “immediately before birth, the gastrointestinal tract of a baby is thought to be sterile” and that during the process of birth, the gastrointestinal tract of a baby “encounters bacteria from the digestive tract and skin of the mother and starts to become colonised.” (Sprenger 2.) Sprenger further notes, like Donnet-Hughes, that “[l]arge differences exist with respect to the

composition of the gut microbiota in response to the infant's feeding" and that breast fed babies include "appreciable populations of bifidobacteria." (*Id.*) Similarly to Donnet-Hughes, Sprenger teaches that *B. lactis* CNCM I-3446<sup>10</sup> in combination with prebiotics "promote[s] the establishment of a bifidogenic intestinal microbiota in infants" (Sprenger 14 and 18 (Example 5, and Figures 3–5)) regardless of whether these infants are neonates, born by c-section or born vaginally, and that adding this to the infant diet "encourage[s] gut colonization to take place and . . . promote[s] colonization with the 'good' bacteria," including bifidobacteria, "rather than the harmful bacteria - pathogens such as clostridia, etc." which are "usually present" in formula fed infants (Sprenger 2–3, 14.) Thus, regardless of Senok's general statement concerning strain specificity of probiotics, one of ordinary skill in the art would reasonably expect *B. lactis* CNCM I-3446 to promote a beneficial intestinal microbiota in infants delivered by c-section or vaginally, and whether neonate or not, in light of the prior art cited by the Examiner.

Appellants' argument that any prima facie case of obviousness has been overcome with evidence of unexpected results (Appeal Br. 9–10) is also unpersuasive. "To be particularly probative, evidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art, and that the difference would not have been expected by one of ordinary skill in the art at the time of the invention."

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<sup>10</sup> Appellants contend that "Sprenger does not teach *B. lactis* CNCM I-3446." (Appeal Br. 8.) We disagree. Sprenger specifically identifies this strain which it also calls "NCC 2818" as the one that was tested in *in vivo* experiments and for which "results are shown in Figures 3, 4 and 5." (Sprenger 18 (Example 5).)

*Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014). Appellants' evidence is deficient on both accounts.

As the Examiner notes, Appellants' evidence is not a comparison to the closest prior art. (Ans. 12–15.) Boehm teaches a composition comprising *B. lactis* among other Bifidobacterium and at least one indigestible oligosaccharide for administration to infants delivered by c-section. (Boehm 18 (Ex. 4).) Boehm's Example 4 thus differs from the method of claim 1 in the strain of *B. lactis* and the specific oligosaccharides recited. Sprenger's Example 5 describes administration of *B. lactis* CNCM I-3446 and an oligosaccharide mixture that comprised "about 30 wt% GalNAc $\alpha$ 1,3Gal $\beta$ 1,4Glc and Gal $\beta$ 1,6GalNAc $\alpha$ 1,3Gal $\beta$ 1,4Glc, 50 wt% of Gal $\beta$ 1,6Gal $\beta$ 1,4Glc and Gal $\beta$ 1,3Gal $\beta$ 1,4Glc and 20 wt% of NeuAca2,3Gal $\beta$ 1,4Glc and NeuAca2,6Gal $\beta$ 1,4Glc." (Sprenger 15:7–9, 18:5–26.) Sprenger's Example 5 thus differs from the method of claim 1 only in the amounts of the recited oligosaccharides and the subjects to whom it was administered (a mouse "model of human infant microbiota" in Sprenger (*id.* at 18:12) versus infants delivered by c-section in claim 1). Appellants' comparison, while being in a mouse model of c-section delivery, did not compare against a mouse model that was provided with a *B. lactis* strain and a galactooligosaccharide taught by Boehm, nor was it a comparison between the composition of Sprenger provided in mouse models reflective of a "model of human infant microbiota" as compared to a mouse model of infants delivered by c-section. Instead, Appellants' comparison is between a group who was initially provided with *B. longum* and given *B.*

*lactis* CNCM I-3446 and CMOS-GOS<sup>11</sup> against a control group that was provided with additional *B. longum*. (Appeal Br. 9–10; Ans. 14.) Appellants’ evidence, therefore, does not show a comparison to the closest prior art.

Moreover, based on the teachings of Boehm, the use of any *B. lactis* strain would have been expected to stimulate the development of a healthy intestinal flora in an infant delivered by c-section, and as discussed above the teaching of Donnet-Hughes and Sprenger would teach one of ordinary skill in the art that *B. lactis* CNCM I-3446 in particular would achieve those results.

Claims 7–9 and 11–15 have not been argued separately and, therefore, fall with claim 1. 37 C.F.R. § 41.37(c)(1)(iv).

#### SUMMARY

For the reasons discussed above, we affirm the rejection of claims 1, 7–9, and 11–15 under 35 U.S.C. § 103(a) as unpatentable over Boehm, Donnet-Hughes, Sprenger, Isolauri, and Masco.

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<sup>11</sup> CMOS-GOS is an oligosaccharide mixture including N-acetylated oligosaccharides, neutral oligosaccharides and sialylated oligosaccharides. (Spec. 16.) The CMOS-GOS used in the examples contains about 9 wt % N-acetylated oligosaccharides, about 82 wt % neutral oligosaccharides and about 9 wt % sialylated oligosaccharides. (Spec. 18.)

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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