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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ROBERTA ONDEI and EDNA FERNANDES

Appeal 2020-000556
Application 15/565,983
Technology Center 1600

Before RICHARD M. LEBOVITZ, JASON V. MORGAN, and DEBORAH KATZ, *Administrative Patent Judges*.

KATZ, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellant[1] seeks our review[2], under 35 U.S.C. § 134(a), of the Examiner's decision to reject claims 1, 3–10 and 15. Claims 2 and 12 were canceled and claims 11, 13, and 14 were withdrawn. We have jurisdiction under 35 U.S.C. § 6(b). We REVERSE.

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[1] We use the word "Appellant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as Croda International PLC. (Appeal Br. 1.)

[2] We consider the Final Office Action issued December 26, 2018 ("Final Act."), the Appeal Brief filed July 26, 2019 ("Appeal Br."), the Examiner's Answer issued on October 7, 2019 ("Ans."), the Reply Brief filed November 1, 2019 ("Reply Br.").

Appellant's Specification is directed to emulsifiers for injectable water in oil emulsions, particularly for use in veterinary vaccines. (Spec. 1:3–4.)

Appellant's claim 1 recites:

> 1. A vaccine formulation comprising a water-in-oil emulsion and at least one vaccine antigen, oil, and water, where said emulsion comprises an emulsifier having a general structure (I):
>
> $R^1 \cdot [(AO)_n – R^2]_m$ (I)
>
> wherein
>
> R^1 is the residue of a polyol or polyamine, each said polyol or polyamine having m active hydrogen atoms, where m is an integer of at least 2;
>
> AO is an oxyalkylene group;
>
> each n independently represents an integer in the range from 1 to 100;
>
> each R^2 independently represents hydrogen, or an acyl group represented by $-C(O)R^3$ wherein each R^3 independently represents a residue of polyhydroxyalkyl carboxylic acid, polyhydroxyalkenyl carboxylic acid, hydroxyalkyl carboxylic acid, hydroxyalkenyl carboxylic acid, oligomer of hydroxyalkyl carboxylic acid, or oligomer of hydroxyalkenyl carboxylic acid; and
>
> wherein on average at least two R^2 groups per molecule are alkanoyl groups as defined.

(Appeal Br. 8.)

The Examiner rejects Appellant's claims 1, 3–10, and 15 under 35 U.S.C. § 103 as obvious over Brancq[3] and Garti.[4] (*See* Final Act. 3–6.)

As the Examiner finds, Brancq teaches an injectable vaccine comprising an oily adjuvant and an emulsifier. (*See* Brancq Abstract; *see* Ans. 3.) Brancq teaches that the emulsifier can be obtained by condensing a fatty acid, such as linoleic and ricinoleic acids, with a sugar, such as mannitol, glucose, sucrose, or with glycerol. (*See* Brancq 5:65–6:2; *see* Ans. 3.) Brancq teaches that the hydrophilicity of the ester can be modified by grafting hydrophilic groups such as ethylene oxide or propylene oxide. (*See* Brancq 6:7–10; *see* Ans. 3.)

Brancq teaches that it was known that the injectibility of oily vaccines could be improved by incorporating a small proportion of the hydrophilic emulsifier, such as polysorbate 80, in an antigen medium. (Brancq 3:4–8.) But Brancq also teaches that it was known that polysorbate 80 attacks the cell wall and so is potentially toxic. (*See id.* at 3:11–13.)

The Examiner finds that Brancq does not teach an integer n for oxyalkylene with an MW 3000–8000. (*See* Final Act. 4.)

Garti teaches microemulsion pharmaceutical compositions that have enhanced permeability and extended release properties. (*See* Garti Abstract; *see* Ans. 4.) Garti lists PEG-40 and PEG-80, among other surfactants, for use in the disclosed pharmaceutical compositions. (*See* Garti ¶ 53; *see* Ans. 4.)

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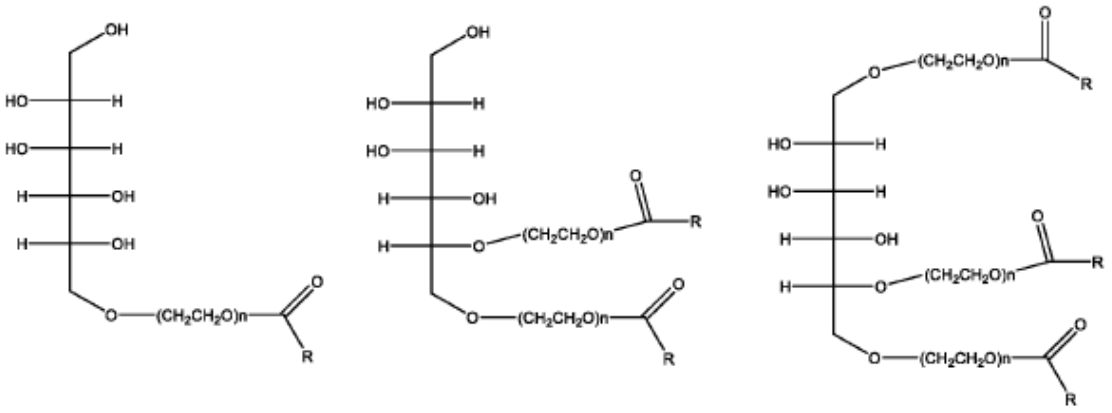
[3] Brancq, US Patent US 5,422,109, issued June 6, 1995.
[4] Garti et al., US Patent Application Publication 2010/0143462 A1, published June 10, 2010.

According to the Examiner, the amount of PEG on polyoxyethylene mannitol ricinoleate could have been optimized through routine experimentation. (*See* Ans. 4.) The Examiner finds that because Garti teaches PEG (40–80) sorbitan fatty acid ester it would have been obvious to one of ordinary skill to have polyoxyethylene mannitol ricinoleate with 40–80 PEG as a surfactant and that there would have been a reasonable expectation of success in achieving the claimed vaccine formulation. (*See* Ans. 4–5.)

Appellant argues that the Examiner erred because claim 1 requires at least two R^2 groups per molecule are alkanoyl groups, but that the polyoxyethylene mannitol ricinoleate with 40–80 PEG proposed by the Examiner is a monoester. (*See* Appeal Br. 5.) Thus, Appellant argues that the polyoxyethylene mannitol ricinoleate with 40–80 PEG proposed by the Examiner does not fall within the scope of claim 1. (*See id.*) Appellant argues further that Brancq fails to teach how or where the hydrophilic groups are grafted, how many hydrophilic groups are grafted, or that at least two alkanoyl groups are present, as specified in claim 1 of the present application. (*See* Ans. 6.)

The Examiner asserts that mono-ricinoleate, di-ricinoleate, and tri-ricinoleate will normally form when PEG groups are grafted on to mannitol ricinoleate. (*See* Ans. 9.) According to the Examiner, Brancq teaches surfactant mannitol, glucose ester with ricinoleic modified with ethylene oxide, but does not expressly indicate how mannitol (glucose) ricinoleate is modified with ethylene oxide. (*See* Ans. 7.) The Examiner finds, though, that because polysorbate 80 was a commonly known surfactant from sorbitan monooleate that could be modified by grafting polyoxyethylene

(PEG) between the hydroxyl of sugar and acyl group, it would have been obvious for one of ordinary skill in the art to modify mannitol (glucose) ricinoleate by similarly grafting PEG between hydroxyl of sugar and acyl group to produce polyoxyethylene mannitol (glucose) ricinoleate. (*See* Ans. 7–8.) The Examiner asserts that because polysorbate 80 was a commonly known surfactant it teaches how PEG groups can be grafted to produce polyoxyethylene mannitol (glucose) ricinoleate and renders it obvious in view of Brancq. (*See* Ans. 8.) The Examiner provides three different example structures of PEG mannitol ricinoleate, which are reproduced below.



(Ans. 9.) Three structures of PEG mannitol ricinoleate are depicted, having either one, two, or three ricinoleate residues.

The Examiner fails to explain, though, why one of ordinary skill in the art would have made the asserted modifications of the compounds taught in Brancq. The Examiner states that "[o]ne of ordinary skill in the art would have been motivated to have polyoxyethylene mannitol ricinoleate with 40-80 PEG because the amount of PEG is adjustable and optimizable under prior art condition or through routing experimentation." (Ans. 4.) Not only

does the Examiner fail to cite support for the optimization of PEG and how such optimization would be achieved, but the Examiner's statement fails to explain why one would undertake such optimization, given that Brancq does not teach at least two R^2 alkanoyl groups. Brancq teaches condensing a fatty acid with a sugar or glycerol and modifying the esters obtained by grafting a hydrophilic group, but the Examiner does not cite to a teaching of how to optimize, control or otherwise achieve any specificity in such reactions. (*See* Brancq 5:65–6:10.)

The Examiner cites to Example 1 of Appellant's Specification to show that an esterification reaction of PEG-50 sorbitol and poly-12-hydroxystearic acid results in sorbitol poly-12-hydroxystearic acid ester that includes di- or tri-ester of PEG-50 sorbitol, but the Appellant's Specification cannot be used as evidence of a reason to make such modifications without resorting to improper hindsight. (*See* Ans. 9.) Furthermore, we agree with Appellant that Example 1 does not teach using ricinoleate diesters or triesters modified with oxyalkylene groups and, thus, fails to show that modification of the compounds of Brancq would necessarily lead to the structure recited in claim 1. (*See* Appeal Br. 6.)

We agree with Appellant that Brancq fails to teach or suggest modification of polyoxyethylene mannitol ricinoleate with 40–80 PEG to achieve a compound with at least two R^2 alkanoyl groups per molecule as required in claim 1. (*See* Appeal Br. 5.) We also agree with Appellant that the mere listing of 40 PEG and 80 PEG in Garti fails to cure this deficiency. (*See* Appeal Br. 6.)

Furthermore, Bracq does not identify the position of the oxyalkylene group when grafted to the mannitol group. The Examine states the it would

be obvious to place it between the sugar and acyl group, but does not provide an adequate reason for doing so. *See* Ans. 7–8.

Accordingly, we are persuaded by Appellant's arguments that the Examiner fails to show that the combination of Brancq and Garti renders the vaccine formulation of claim 1 obvious. Because claims 3–10 and 15 depend on claim 1, we are also persuaded that the Examiner fails to show that these claims are obvious.

CONCLUSION

Upon consideration of the record and for the reasons given, we reverse the Examiner's rejection.

In summary:

Claims Rejected	**35 U.S.C. §**	**References**	**Affirmed**	**Reversed**
1, 3–10, 15	103	Brancq, Garti		1, 3–10, 15

REVERSED