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Paper 12
Entered: July 12, 2017

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FAMY CARE LIMITED,
Petitioner,

v.

ALLERGAN, INC.,
Patent Owner.

Case IPR2017-00566
Patent 8,648,048 B2

Before SHERIDAN K. SNEDDEN, TINA E. HULSE, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges.*

SNEDDEN, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review and Denying Motion for Joinder
35 U.S.C. § 315(c); 37 C.F.R. § 42.108

I. INTRODUCTION

Famy Care Limited ("Famy Care" or "Petitioner") filed a Petition to institute an *inter partes* review of claims 1–23 (Paper 3; "Petition" or "Pet.") of US 8,648,048 B2 (Ex. 1001; "the '048 patent"). Allergan, Inc. ("Allergan" or "Patent Owner") did not file a Preliminary Response to the Petition.

Petitioner also filed a Motion for Joinder pursuant to 35 U.S.C. § 315(c), seeking to join this proceeding with *Mylan Pharmaceuticals, Inc. v. Allergan, Inc.*, IPR2016-01131 ("Mylan IPR"). Paper 5. Patent Owner opposes Petitioner joinder motion. Paper 9. For the reasons stated below, we deny Petitioner's motion for joinder.

As for the Petition, we have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Upon consideration of the Petition, we determine that Petitioner has established a reasonable likelihood that it will prevail with respect to at least one of the challenged claims. We institute an *inter partes* review as to claims 1–23 of the '048 patent.

A. Related Proceedings

The parties identify petitions for *inter partes* review previously filed by other petitioners that challenge the claims of the '048 patent and related patents. Pet. 4–5; Paper 8, 2–3. Certain petitions were terminated before decisions on institution were entered. Pet. 5; Paper 6, 2. Other petitions have been granted and *inter partes* review has been instituted for the following U.S. Patents: U.S. Patent No. 8,633,162 (IPR2016-01130,

IPR2017-00568, IPR2017-00599, IPR2017-00583); U.S. Patent No. 8,685,930 (IPR2016-01127, IPR2017-00571, IPR2017-00594, IPR2017-00576); U.S. Patent No. 8,629,111 (IPR2016-01128, IPR2017-00567, IPR2017-00596, IPR2017-00578); U.S. Patent No. 8,642,556 (IPR2016-01129 IPR2017-00570, IPR2017-00598, IPR2017-00579); U.S. Patent No. 8,648,048 (IPR2016-01131, IPR2017-00600, IPR2017-00585); and U.S. Patent No. 9,248,191 (IPR2016-01132, IPR2017-00569, IPR2017-00601, IPR2017-00586). Paper 6, 2–3.

B. The '048 patent (Ex. 1001)

The '048 patent generally relates to methods of providing therapeutic effects using cyclosporin components, and more specifically to a formulation containing, *inter alia*, cyclosporin-A ("CsA") and castor oil emulsions for treating dry eye syndrome (i.e., keratoconjunctivitis sicca). Ex. 1001, 2:55–3:11. According to the specification, the prior art recognized the use of emulsions containing CsA and CsA derivatives to treat ophthalmic conditions. *Id.* at 1:26–65. The specification notes, however, that "[o]ver time, it has been apparent that cyclosporin A emulsions for ophthalmic use preferably have less than 0.2% by weight of cyclosporin A." *Id.* at 1:66–2:2. Moreover, if reduced amounts of CsA are used, reduced amounts of castor oil are needed because one of the functions of castor oil is to solubilize cyclosporin A. *Id.* at 2:1–2:6.

Accordingly, the specification states that "[i]t has been found that the relatively increased amounts of hydrophobic component together with relatively reduced, yet therapeutically effective, amounts of cyclosporin component provide substantial and advantageous benefits." *Id.* at 2:35–38. The relatively high concentration of hydrophobic component provides for a

more rapid breaking down of the emulsion in the eye, which reduces vision distortion and/or facilitates the therapeutic effectiveness of the composition. *Id.* at 2:42–48. Furthermore, using reduced amounts of cyclosporin component mitigates against undesirable side effects or potential drug interactions. *Id.* at 2:48–51.

The patent identifies two particular compositions that were selected for further testing, as shown below:

	Composition I wt %	Composition II wt %
Cyclosporin A	0.1	0.05
Castor Oil	1.25	1.25
Polysorbate 80	1.00	1.00
Premulen ®	0.05	0.05
Glycerine	2.20	2.20
Sodium hydroxide	qs	qs
Purified Water	qs	qs
pH	7.2-7.6	7.2-7.6
Weight Ratio of Cyclosporin A to Castor Oil	0.08	0.04

Id. at 14:15–30. Based on the results of a Phase III clinical study, the specification concludes that "Composition II . . . provides overall efficacy in treating dry eye disease substantially equal to that of Composition I." *Id.* at 14:35–40. The patent indicates that "[t]his is surprising for a number of reasons." *Id.* at 14:41. According to the specification, a reduced concentration of CsA in Composition II would have been expected to result in reduced overall efficacy in treating dry eye disease. *Id.* at 14:41–44. Moreover, although the large amount of castor oil relative to the amount of CsA in Composition II might have been expected to cause increased eye irritation, it was found to be substantially non-irritating in use. *Id.* at 14:44–49. Accordingly, the specification states that physicians can prescribe Composition II "to more patients and/or with fewer restrictions and/or with reduced risk of the occurrence of adverse events, e.g., side effects, drug

interactions and the like, relative to providing Composition I." *Id.* at 15:4–8.

C. The Asserted Grounds

Petitioner challenges claims 1–23 of the '048 patent on the following grounds. Pet. 6–7.

Ground	Reference[s]	Basis	Claims challenged
1	Ding '979 [1]	§ 103	1– 23
2	Ding '979 and Sall[2]	§ 103	1– 23
3	Ding '979, Sall, and Acheampong[3]	§ 103	11 and 21
4	Ding '979, Sall, and Glonek[4]	§ 103	15

Petitioner also relies on the Declarations of Peter Kador, Ph.D. (Ex. 1002) and Michael Lemp, M.D. (Ex. 1003).

D. Illustrative Claims

Independent claims 1, 18, and 22 are illustrative of the challenged claims, and are reproduced below:

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[1] Ding et al., U.S. Patent No. 5,474,979, issued December 12, 1995 (Ex. 1006, "Ding '979").

[2] Kenneth Sall et al., *Two Multicenter, Randomized Studies of the Efficacy and Safety of Cyclosporine Ophthalmic Emulsion in Moderate to Severe Dry Eye Disease*, 107 OPHTHALMOLOGY 631–639 (2000) (Ex. 1007, "Sall").

[3] Andrew Acheampong et al., *Cyclosporine Distribution Into The Conjunctiva, Cornea, Lacrimal Gland, And Systemic Blood Following Topical Dosing Of Cyclosporine To Rabbit, Dog, And Human Eyes, in* LACRIMAL GLAND, TEAR FILM, AND DRY EYE SYNDROMES 2, BASIC SCIENCE AND CLINICAL RELEVANCE, 1001–1004 (1998) (Ex. 1008, "Acheampong").

[4] Glonek et al., U.S. Patent No. 5,578,586, issued Nov. 26, 1996. Ex. 1009 ("Glonek").

1. A method of increasing tear production in the eye of a human, the method comprising topically administering to the eye of the human in need thereof an emulsion at a frequency of twice a day, wherein the emulsion comprises cyclosporin A in an amount of about 0.05% by weight, polysorbate 80, acrylate/C10–30 alkyl acrylate cross-polymer, water, and castor oil in an amount of about 1.25% by weight; and

wherein the topical ophthalmic emulsion is effective in increasing tear production.

18. A method of treating keratoconjunctivitis sicca, the method comprising the step of topically administering to an eye of a human in need thereof an emulsion at a frequency of twice a day, the emulsion comprising:

cyclosporin A in an amount of about 0.05% by weight;

castor oil in an amount of about 1.25% by weight;

polysorbate 80 in an amount of about 1.0% by weight;

acrylate/C10–30 alkyl acrylate cross-polymer in an amount of about 0.05% by weight;

a tonicity component or a demulcent component in an amount of about 2.2% by weight;

a buffer; and

water;

wherein the emulsion is effective in treating keratoconjunctivitis sicca and wherein the topical ophthalmic emulsion has a pH in the range of about 7.2 to about 7.6.

22. A method comprising:

administering an emulsion topically to the eye of a human having keratoconjunctivitis sicca at a frequency of twice a day, wherein the emulsion comprises:

cyclosporin A in an amount of about 0.05% by weight;

castor oil in an amount of about 1.25% by weight;

polysorbate 80 in an amount of about 1.0% by weight;

acrylate/C10–30 alkyl acrylate cross-polymer in an amount of about 0.05% by weight;

glycerine in an amount of about 2.2% by weight;

sodium hydroxide; and

water; and

> wherein the emulsion is effective in increasing tear production in the human having keratoconjunctivitis sicca.

Claims 2–17 depend from claim 1, either directly or indirectly. Claims 19–21 depend from claim 18, either directly or indirectly. Claim 23 depend from claim 22, either directly or indirectly.

II. ANALYSIS

A. Motion for Joinder

Based on authority delegated to us by the Director, we have discretion to join an *inter partes* review to a previously instituted *inter partes* review. 35 U.S.C. § 315(c). Section 315(c) provides, in relevant part, that "[i]f the Director institutes an inter partes review, the Director, in his or her discretion, may join as a party to that inter partes review any person who properly files a petition under section 311." *Id.* When determining whether to grant a motion for joinder we consider factors such as timing and impact of joinder on the trial schedule, cost, discovery, and potential simplification of briefing. *Kyocera Corp. v. SoftView, LLC*, Case IPR2013-00004, slip op. at 4 (PTAB Apr. 24, 2013) (Paper 15).

Although Famy Care's Petition is similar to Mylan's Petition in terms of the art relied for each patentability challenge, it is not a "me-too" petition and differs significantly in its presentation of arguments. For example, Famy Care's Petition challenges claims 1–23 over Ding '979 and Sall, whereas Mylan's Petition challenges claims 1–10, 12–14, 16–20, 22, and 23 over the same art. *Compare* Pet. 6 *with* Mylan Pet.[5] 13. Famy Care relies

[5] Mylan IPR, Petition for Inter Partes Review of U.S. Patent No. 8,633,162 Paper 3 (filed June 3, 2016) ("Mylan Pet.").

upon the declarations of Dr. Peter Kador (Ex. 1002) and Dr. Michael A. Lemp (Ex. 1003) to support its Petition, whereas Mylan relies upon the declaration of Mansoor Amiji, Ph.D. Famy Care also presents extensive additional arguments and evidence regarding secondary considerations. Pet. 56–77.

Allergan asserts that there are "significant differences between Famy Care's petition and Mylan's petition." Paper 9, 2. Nevertheless, Allergan indicated that it will not oppose joinder if Famy Care agrees to participate in the joined proceedings under the following conditions:

> 1. Famy Care agrees to rely solely on Mylan's expert;
>
> 2. Famy Care agrees to consolidated briefing subject to the word count limits for a single party except for motions that involve only Famy Care;
>
> 3. Famy Care agrees that cross-examination of Patent Owner's witnesses will occur within the timeframe that the rules allot for one party; and
>
> 4. Famy Care agrees that Mylan will conduct the oral argument.

Paper 9, 2.

In its Reply in support of the Motion for Joinder, Famy Care indicates that it only agrees to one of Allergan's conditions—to conduct the cross-examination of Patent Owner's witnesses within the timeframe allotted for one party. Paper 10, 1. Famy Care, however, states that it cannot agree to forgo reliance on its expert declarants because its experts "include a distinguished clinician who can provide the Board a valuable perspective on the secondary considerations arguments Allergan leans heavily on." *Id.* at 2–3. Famy Care also asserts that it cannot agree to limit its briefing in the

joined proceeding on the basis that it "believes additional briefing, including on its secondary considerations arguments, will give [Famy Care] a fair chance to present its own arguments and aid the Board in considering the instituted grounds." *Id.* at 4. Famy Care only agrees to "consolidate its briefing with Mylan if permitted separate briefing of up to seven pages (including but not limited to arguments on which Mylan lacks standing, or [Famy Care] and Mylan disagree)." *Id.* Finally, with respect to oral arguments, Famy Care agrees to have Mylan argue first, but asserts a right to "present its own arguments (if necessary) only on issues where the Petitioners disagree, or where Mylan has no standing to address, all within the allotted time for one party." *Id.* at 3.

Under the circumstances, we determine that joinder of Famy Care to IPR2016-01131 is not appropriate. Famy Care argues that if an *inter partes* review is instituted based on its Petition, "but joinder is denied, Allergan would be compelled to go through duplicative discovery to defend against two IPR petitions, and the Board would be required to consider similar arguments on the same ground twice." *Id.* at 4. As noted above, however, Famy Care does not concede to simply taking a "silent understudy" role with respect to Mylan, and instead seeks the opportunity to present additional arguments, briefing, and evidence, including two additional expert declarations, beyond what is being considered based on Mylan's Petition in IPR2016-01131. Moreover, to the extent that a denial of joinder would result in duplicative proceedings for Allergan, we note that Allergan has opposed joinder in this instance. Accordingly, we determine that joinder under these conditions would not "secure the just, speedy, and inexpensive

resolution" of the proceeding. *See* 37 C.F.R. § 42.1(b). Thus, Famy Care's Motion for Joinder is denied.

Having determined that joinder is not appropriate, we now consider Famy Care's Petition on the merits.

B. Claim Interpretation

We interpret claims using the "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs. LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under the broadest reasonable construction standard, claim terms are given their "ordinary and customary meaning," as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007) (quoting *Phillips v. AWH Corp*, 415 F.3d 1303, 1312 (Fed. Cir. 2006)). "Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaim[s] the broader definition." *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004) (citation omitted). "Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

1. "effective"/"therapeutically effective"

Claims 1–17 and 22–23 recite that the emulsion is "effective in increasing tear production," whereas claims 18–21 recite an emulsion that is "effective in treating keratoconjunctivitis sicca." The dependent claims recite other variations such as an emulsion that is "substantially

therapeutically effective as a second emulsion" or achieves "at least as much therapeutic effectiveness as a second emulsion."

Petitioner asserts that the plain meaning of the word "therapeutic" includes palliative as well as curative treatments, and as such, emulsions effective in increasing tear production is an example of an emulsion therapeutically effective in treating dry eye disease/KCS palliative and curative treatments. Pet. 18–19 (citing Ex. 1002 ¶¶ 70; Ex. 1003 ¶¶ 82–83, 85; Ex. 1022, 4–5, 7). We agree that, on the current record, the ordinary meaning of the phrase "therapeutically effective" and similar phrases includes palliative effects. That being said, at this stage of the proceeding, we find that "effective in increasing tear production" does not require further construction as its meaning is clear on its face. We also find that "effective in treating keratoconjunctivitis sicca" encompasses both the treatment of the symptoms of dry eye disease as well as the disease itself.

2. Remaining Claim Terms

We determine that no explicit construction of any claim term is necessary to determine whether to institute a trial in this case. *See, e.g.*, *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

At this stage of the proceeding, we have not made a final determination as to the construction of any claim term.

C. Principles of Law

We analyze the proposed grounds of unpatentability in accordance with the following stated principles.

A patent may not be obtained if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. 35 U.S.C. § 103(a). The legal question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness, i.e., secondary considerations. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

In *KSR International Co. v. Teleflex Inc.*, the Supreme Court stated that an invention may be found obvious if trying a course of conduct would have been obvious to a person having ordinary skill:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

550 U.S. 398, 421 (2007). "*KSR* affirmed the logical inverse of this statement by stating that § 103 bars patentability unless 'the improvement is more than the predictable use of prior art elements according to their established functions.'" *In re Kubin*, 561 F.3d 1351, 1359–60 (Fed. Cir. 2009) (citing *KSR*, 550 U.S. at 417).

The factual inquiries for an obviousness determination also include secondary considerations based on evaluation and crediting of objective

evidence of nonobviousness. *Graham*, 383 U.S. at 17–18. Notwithstanding what the teachings of the prior art would have suggested to one with ordinary skill in the art at the time of the invention, the totality of the evidence submitted, including objective evidence of nonobviousness, may lead to a conclusion that the claimed invention would not have been obvious to one with ordinary skill in the art. *In re Piasecki*, 745 F.2d 1468, 1471–72 (Fed. Cir. 1984).

Such a conclusion, however, requires the finding of a nexus to establish that the evidence relied upon traces its basis to something novel in the claim and not to something in the prior art. *Institut Pasteur & Universite Pierre et Marie Curie v. Focarino*, 738 F.3d 1337, 1347 (Fed. Cir. 2013). Generally, objective evidence of nonobviousness must be shown to have a nexus. *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) (nexus generally); *In re Kao*, 639 F.3d 1057, 1069 (Fed. Cir. 2011) (unexpected results); *In re Huang*, 100 F.3d 135, 140 (Fed. Cir. 1996) (commercial success); *Rambus Inc. v. Rea*, 731 F.3d 1248, 1256 (Fed. Cir. 2013) (long-felt need).

Objective evidence of nonobviousness also must be reasonably commensurate in scope with the claim. *Kao*, 639 F.3d at 1068. This does not mean that the proffered evidence must reach every embodiment within the scope of the claim, so long as there is an "adequate basis to support the conclusion that other embodiments falling within the claim will behave in the same manner." *Id.*

D. Content of the Prior Art

Petitioner relies upon the following prior art in its challenges.

1. Ding '979 (Ex. 1006)

Ding '979, assigned to Patent Owner, relates to ophthalmic emulsions including cyclosporin, castor oil, and polysorbate 80 that have a high comfort level and low irritation potential. Ex. 1006, cover, 1:4–9. Ding '979 explains that cyclosporins have "known immunosuppressant activity" and have been found "effective in treating immune medicated keratoconjunctivitis sicca (KCS or dry eye disease) in a patient suffering therefrom." *Id.* at 1:10–16. Although the solubility of cyclosporins in water is extremely low, cyclosporins have some solubility in oily preparations containing higher fatty acid glycerides such as castor oil. *Id.* at 1:40–41, 2:39–42. Ding '979 notes, however, that formulations with a high concentration of oils have several drawbacks, including exacerbation of the symptoms of dry eyes and low thermodynamic activity of cyclosporin, which leads to poorer drug bioavailability. *Id.* at 2:42–57. Accordingly, Ding '979 "is directed to an emulsion system which utilizes higher fatty acid glycerides but in combination with polysorbate 80 which results in an emulsion with a high comfort level and low irritation potential suitable for delivery of medications to sensitive areas such as ocular tissues." *Id.* at 2:65–3:3.

Ding '979 discloses that the preferable weight ratio of CsA to castor oil is below 0.16, and more preferably between 0.12 and 0.02. *Id.* at 3:15–20. Specifically, Ding '979 discloses several compositions as Example 1, shown below:

Example 1					
	A	B	C	D	E
Cyclosporin A	0.40%	0.20%	0.20%	0.10%	0.05%
Castor oil	5.00%	5.00%	2.50%	1.25%	0.625%
Polysorbate 80	1.00%	1.00%	1.00%	1.00%	1.00%
Pemulen ®	0.05%	0.05%	0.05%	0.05%	0.05%
Glycerine	2.20%	2.20%	2.20%	2.20%	2.20%
NaOH	qs	qs	qs	qs	qs
Purified water	qs	qs	qs	qs	qs
pH	7.2–7.6	7.2–7.6	7.2–7.6	7.2–7.6	7.2–7.6

Id. at 4:32–43. Example 1 identifies compositions A through E, which contain varying amounts of CsA, castor oil, polysorbate 80, Pemulen®(an acrylate/C10-30 alkyl acrylate cross-polymer) (*id.* at 4:1–5), glycerine, sodium hydroxide, and purified water at a pH range of 7.2–7.6. *Id.* at 4:32–43. According to Ding '979, the formulations of Example 1 was "made for treatment of keratoconjunctivitis sicca (dry eye) syndrome." *Id.* at 5:10–12.

2. Sall (Ex. 1007)

Sall describes the results of two identical clinical trials—supported by a grant from Patent Owner—in which patients were treated twice daily with either CsA 0.05% or 0.1% ophthalmic emulsions or vehicle for six months. Ex. 1007, Abstract, 631. The study sought to compare the efficacy and safety of CsA 0.05% and 0.1% to vehicle in patients with moderate to severe dry eye disease. *Id.* Sall found that "topical treatment with either CsA 0.05% or 0.1% resulted in significantly greater improvements than vehicle treatment in two objective signs of dry eye disease." *Id.* at 637. Sall also found that treatment with CsA 0.05% resulted in significantly greater improvements in several subjective parameters. *Id.* Sall also found that trough blood concentrations of CsA were undetectable in all samples of CsA

0.05%, whereas CsA was quantifiable in only six samples for six different patients in the CsA 0.1% group. *Id.*

Sall notes that the only treatments available for dry eye disease are palliative in nature. *Id.* at 638. In light of the results of the study, Sall states that it "represents the first therapeutic treatment specifically for dry eye disease and a significant breakthrough in the management of this common and frustrating condition." *Id.*

3. Acheampong (Ex. 1008)

Acheampong describes a study by Patent Owner as part of its evaluation of the clinical efficacy of 0.05%–0.4% cyclosporin emulsion for the treatment of immuno-inflammatory eye diseases such as dry eye syndrome. Ex. 1008, 1001. Acheampong describes the results of its research to determine the ocular tissue distribution of cyclosporin in rabbits and dogs, and to compare tissue concentrations in rabbits, dogs, and humans after topical administration. *Id.*

In the study of humans, the subjects with dry eye disease received an eyedrop of vehicle or 0.05%, 0.1%, 0.2%, or 0.4% cyclosporin emulsions twice daily for 12 weeks. *Id.* at 1002. Blood samples were collected from all subjects at morning troughs after 1, 4, and 12 weeks of dosing, and from certain subjects at 1, 2, and 4 hours after the last dose at week 12. *Id.* Acheampong found that the human blood cyclosporin A concentrations were less than 0.2 ng/ml for each emulsion, which is lower than the 20–100 ng/ml blood trough concentration used for monitoring the safety of patients receiving systemic cyclosporin therapy. *Id.*

4. Glonek (Ex. 1009)

Glonek relates to a composition for augmenting and maintaining a stable tear film over the ocular surface and delivering a medicine to the eye without causing substantial blurring of vision. Ex. 1009, 1:21–29. Glonek explains that an emulsion over the surface of the eye is expected to cause blurring, which is likely to occur until the emulsion differentiates. *Id.* at 6:37–42. If the emulsion is too stable, excess emulsion will be discharged from the eye. *Id.* at 6:42–44. Thus, Glonek states that it is preferred that an emulsion be stable for long term storage, but rapidly differentiate in the eye. *Id.* at 6:48–50.

E. Asserted Grounds of Unpatentability

1. Obviousness of Claims 1–23 Based on Ding '979 and Sall

Petitioner contends that claims 1–23 are rendered obvious by the combined teachings of Ding '979 and Sall. Pet. 29–52. Petitioner sets forth the foregoing teachings of Ding '979 and Sall and provides a detailed discussion and claim charts explaining how each claim limitation of the challenged claims is disclosed in Ding '979 and/or Sall. *Id.* The issue before us is whether it would have been obvious to use the particular concentrations of 0.05% CsA and 1.25% castor oil recited in the challenged claims. *Id.*

In its Example 1, Ding '979 specifically identifies several examples (Examples 1A–1E) that include 0.05% CsA and 1.25% castor oil, albeit not as part of the same composition. Pet. 29; Ex. 1006, 4:32–43; Ex. 1002 ¶ 156. Petitioner contends that:

> The CsA/castor oil amounts in the claimed combination, i.e., 0.05% CsA and 1.25% castor oil, would have been obvious

> to an ordinarily-skilled artisan because the CsA/castor oil ratio of such formulation uses the identical ratio Ding '979 Example 1B (0.04) used, and applies it to a CsA species amount recited in Ding '979 claim 8 and in Ding '979 Example 1E. See EX1002, ¶158; EX1006, 4:33-43, 6:35-41. Applying this ratio also yields a specific castor oil amount that same Example 1 also used. EX1006, 4:33-43 (Example 1D).

Pet. 31. Petitioner further contends that:

> the ordinarily-skilled artisan, seeking to prepare Ding '979 formulations within the scope of claim 8, would retain all Example 1 fixed-formulation elements (e.g., Polysorbate 80 surfactant, Pemulen®, glycerine, NaOH, water), as-is; and consider the Example's existing specific CsA amounts (0.05%, 0.1%, 0.2%, 0.4%), and castor oil amounts (5%, 2.5%, 1.25% and 0.625%). The specific ratios to use of CsA to castor oil would be those the Examples already used (0.04 and 0.08), while staying within the overall claim 8 ingredient preferences (e.g., not more than 5% by weight castor oil). The ordinarily-skilled artisan would be motivated to pursue, reasonably expect to prepare, and ultimately use such formulations for dry eye disease.

Id. at 32.

In an alternate ground, Petitioner combines Ding '979 with Sall and contends that "Sall would have motivated [the ordinarily-skilled artisan] person to make and use the 0.05% CsA emulsion with 1.25% castor oil taught by Ding '979." *Id.* at 33 (citing Ex. 1002, ¶¶ 166-68). Petitioner contends that Sall reports Phase 3 clinical trial results showing that either the 0.05% or 0.10% CsA emulsion is therapeutically effective in increasing tear production and treating dry eye disease/KCS. *Id.* at 33–34 (citing Ex. 1007, 1–2, 7–8; EX1002 ¶ 166; Ex. 1003 ¶98–121).

Petitioner further contends that:

> The combined teachings of Sall and Ding '979 would have led the ordinarily-skilled artisan to a 0.05% CsA and 1.25% castor oil emulsion. An ordinarily-skilled artisan would select the lowest effective dose (0.05% CsA) since Sall reported that there was no dose response effect; and because the 0.05% CsA emulsion appeared to perform better than the 0.1% CsA emulsion. Such person also was motivated to keep blood CsA levels as low as possible, while maintaining efficacy because CsA had known, broad-based immunosuppressant activities. EX1006, 1:67-2:4; EX1007-0001, 0006-07; EX1002, ¶169.

Id. at 35–36.

Based on the arguments presented and evidence of record, we determine that Petitioner has demonstrated a reasonable likelihood that claims 1–23 are obvious over the teachings of Ding '979 alone or in combination with Sall. *See In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003) ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Boesch*, 617 F.2d 272, 276 (CCPA 1980) ("[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art.").

2. Obviousness of Claims 11 and 21 over the Combination of Ding '979, Sall, and Acheampong

Petitioner asserts that claims 11 and 21 are unpatentable as obvious over Ding '979, Sall, and Acheampong. Pet. 53–54. Claims 11 and 21 depend directly from claims 1 and 18 and further recite as follows: "wherein, when the emulsion is administered to the eye of a human in an

effective amount in treating keratoconjunctivitis sicca, the blood of the human has substantially no detectable concentration of the cyclosporin A."

We incorporate here our discussion above regarding the teachings of Ding '979 and Sall. With regard to the elements of claims 11 and 12,

Petitioner asserts that "Acheampong and Sall together teach and give the ordinarily-skilled artisan a reasonable expectation that twice daily administration of 0.05% CsA yields 'substantially no detectable concentration of cyclosporin A' in the blood." Pet. 54 (citing Ex. 1002 ¶ 229; Ex. 1003 ¶¶ 159-60. To support this position, Petitioner asserts as follows:

> Sall states that humans receiving ophthalmic administrations of 0.05% CsA emulsions containing castor oil twice a day had, "[t]rough blood concentrations of CsA . . . below the limit of quantitation (of 0.1 ng/ml) in all samples." EX1007-0007. Acheampong additionally reports on the months-long study evaluating both peak and trough concentrations of CsA in the blood of humans receiving ophthalmic administrations of CsA/castor oil emulsions. EX1008-0004 ("[S]ubjects with KCS received an eyedrop of vehicle or 0.05%, 0.10%, 0.20% or 0.40% cyclosporine emulsion twice daily … Blood samples were collected … at morning troughs … [and] after the last dose [(trough levels)]."). Acheampong Table 1 shows that 0.05% CsA produced no detectable concentration of CsA in the blood at both peak and trough levels.

Id. at 53.

Based on the arguments presented and evidence of record, we determine that Petitioner has demonstrated a reasonable likelihood that

claims 11 and 21 are obvious over the teachings of Ding ’979, Sall, and Acheampong.

3. Obviousness of Claim 15 over the Combination of Ding ’979, Sall, and Glonek

Claim 15 depends from claim 1, and further recites that “the emulsion breaks down more quickly in the eye of a human, . . . thereby reducing vision distortion in the eye of the human as compared to a second emulsion that contains only 50% as much castor oil.”

Petitioner asserts that Glonek discloses emulsions formulated so “blurred vision is reduced or eliminated and the residence time of tear film on the eye is prolonged.” Pet. 55 (citing Ex. 1009, 3:3–7; Ex. 1002 ¶ 233). Petitioner asserts that Glonek discloses that “[t]he duration of the blurring is dependent upon the time required for the emulsion to differentiate and form separate layers.” *Id.* (citing Ex. 1009, 6:37–40; Ex. 1002 ¶ 219). Petitioner asserts that Glonek discloses that “it is preferred that the emulsion be stable for long term storage, but rapidly differentiate in the eye.” *Id.* at (citing Ex. 1009, 6:48–50; Ex. 1002 ¶ 234; Ex. 1003 ¶ 167. Petitioner provides the following rationale to supports its case for obviousness:

> The ordinarily-skilled artisan thus understood that increasing the oil concentration in an emulsion, while holding the surfactant concentration constant, results in an increase in *in vivo* emulsion instability, i.e., an increased rate of differentiation. EX1009, 10:66-11:3, 20:24-31; EX1002, ¶235.
>
> Given Glonek, such person would reasonably expect a 1.25% castor oil emulsion to break down in vivo into its differentiated eye layers faster and reduce blurred vision in comparison to an otherwise identical 0.625% castor oil emulsion, and the increased instability from the higher oil concentration

> would be expected to result in faster differentiation and a reduction of blurring. EX1002, ¶235; EX1003, ¶¶164-69.

Id. at 55–56.

Based on the arguments presented and evidence of record, we are persuaded on the current record that Petitioner has demonstrated a reasonable likelihood that it would prevail in its assertion that claim 15 is unpatentable as obvious over the combination of Ding ’979, Sall, and Glonek.

III. CONCLUSION

We conclude that Petitioner has established a reasonable likelihood of prevailing on its assertions that claims 1–23 of the ’048 patent are unpatentable as obvious.

At this stage of the proceeding, the Board has not made a final determination as to the patentability of any challenged claim or the construction of any claim term.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted on the following grounds:

A. Claims 1–23 as obvious over Ding ’979;

B. Claims 1–23 as obvious over the combination of Ding ’979 and Sall;

C. Claims 11 and 21 as obvious over the combination of Ding ’979, Sall, and Acheampong; and

D. Claim 15 as obvious over the combination of Ding ’979, Sall, and

Glonek.

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this decision; and

FURTHER ORDERED that Famy Care's Motion for Joinder with IPR2016-01131 is *denied*.

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