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EXHIBIT A

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

JARROW FORMULAS, INC.
Respondent and Requester

v.

SOFT GEL TECHNOLOGIES, INC.
Patent Owner and Appellant

Appeal 2015-007926
Reexamination Control 95/002,405
Patent 8,105,583 B2
Technology Center 3900

Before CHUNG K. PAK, RICHARD M. LEBOVITZ, and JEFFREY B. ROBERTSON, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on the appeal by Patent Owner from the Patent Examiner's final rejection of claims 1, 2, 4, 6–10, 12, 13, and 15–17 in the above-identified *inter partes* reexamination of United States Patent 8,105,583 B2. The Board's jurisdiction for this appeal is under 35 U.S.C. §§ 6(b), 134, and 315 (pre-AIA). We affirm.

EXHIBIT A

STATEMENT OF THE CASE

The patent in dispute in this appeal is United States Patent 8,105,583 B2 ("the '583 patent") which issued January 31, 2012.

Jarrow Formulas, Inc. ("Requester") requested *inter partes* reexamination of the '583 patent under 35 U.S.C. §§ 311–318 and 37 C.F.R. §§ 1.902–1.997. Request for *Inter Partes* Reexamination dated September 15, 2012 ("Request"). Reexamination was ordered Nov. 23, 2012. The Action Closing Prosecution was mailed July 3, 2013, and a Right of Appeal Notice ("RAN") mailed April 30, 2014 listed pending claims 1, 2, 4, 6–10, 12, 13, and 15–17 as finally rejected.

Patent Owner, Soft Gel Technologies, Inc., who is the real party in interest, appeals the Examiner's final rejection of these claims. Appeal Br. 1. Patent Owner is the Appellant in this appeal. Requester is the Respondent. An oral hearing was heard on December 9, 2015. A written transcript will be entered into the record in due course.

There are related appeals and trials. Patent Owner identifies two District Court actions related to the current reexamination which involves U.S. Patent 7,588,786 ("Khan '786") [1]: Civil Action No. 2:10-cv-08301-PSG-JCx (C.D. Cal.) and Civil Action No. 2:11-cv-00164-PSG-JCx (C.D. Cal.). Appeal Br. 1. The above Civil Actions were consolidated and the District Court granted summary judgment of noninfringement. The decision was appealed to the Federal Circuit

[1] U.S. Patent No. 7,588,786 B2, issued September 15, 2009, to Mansoor A. Khan and Sami Nazzal. Khan '786 is the basis of anticipation and obviousness rejections in this appeal.

which affirmed the judgment under Fed. Cir. R. 36 (entered Oct. 8, 2014) (2014-1020, -1033, -1039).

There are also two related *inter partes* reexaminations which have been appealed to the Patent Trial and Appeal Board ("PTAB"). A decision affirming the Examiner in Appeal 2015-004072 of Reexamination Control 95/002,411, US Patent 8,147,826 B2, was entered Aug. 31, 2015. A decision in the second appeal, 2015-007397, in Reexamination Control 95/002,396 of US Patent 8,124,072, is entered concurrently with the decision in this appeal. The decisions in this appeal are highly pertinent to the decision in Appeal 2015-004072 as they involve related issues and the same prior art. For this reason, we consider our findings and determinations in this appeal applicable, when relevant, to Appeal 2015-004072.

Claim

Claim 1 is the only independent claim on appeal and reads as follows (underlining and brackets indicate amendments relative to the original claims):

> 1. (Amended) A solubilized coenzyme Q-10 composition comprising: coenzyme Q-10; a sufficient quantity of <u>d-</u>[a]limonene [or a derivative]suitable to solubilize said coenzyme Q-10 thereby providing a solution in which the coenzyme Q-10 remains solubilized, with the proviso that said solution is not part of an emulsion, suspension, or elixir.

Rejections

In the Right of Notice of Appeal, the Examiner rejected claims as follows:

1. Claims 1, 2, 6-10, and 15 under 35 U.S.C. § 102(e) as anticipated by Khan '786, or under 35 U.S.C. § 102(a) as anticipated by Khan '927, as evidenced[2] by Fenaroli,[3] Duetz (Exhibit B),[4] Mondello (Exhibit C),[5] and IARC (Exhibit D).[6] RAN 7.

2. Claims 1, 2, 6-10, and 15 under 35 U.S.C. § 102(b) as anticipated by Nazzal, as evidenced by Fenaroli, Duetz (Exhibit B), Mondello (Exhibit C), and IARC (Exhibit D). RAN 9.

3. Claims 1, 2, 4, 6-10, and 15 under 35 U.S.C. § 103(a) as obvious in view of Khan '786, Nazzal, Fenaroli, Duetz (Exhibit B), Mondello (Exhibit C), and IARC (Exhibit D). RAN 10.

4. Claims 1, 2, 4, 6-10, 12, 13, and 15 under 35 U.S.C. § 103(a) as obvious in view of Motoyama,[7] Patent Owner's Admissions on Motoyama,[8] Khan '786, and Nazzal, as evidenced by Fenaroli, Duetz (Exhibit B), Mondello (Exhibit C),

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[2] The Examiner also cited Exhibits E and F, but we have not relied upon them and therefore do not include them in the ground of rejection or in grounds of rejection 2–4.

[3] Giovanni Fenaroli, Fenaroli's Handbook of Flavor Ingredients, vol. 1, p. 389, 2nd edition, CRC Press, Inc. 1975.

[4] Wouter A. Duetz et al, "Biotransformation of D-Limonene to (+) *trans*-Carveol by Toluene-Grown *Rhodococcus opacus* PWD4 Cells," 67(6) Applied Environmental Microbiology 2829–2832 (June 2001).

[5] Luigi Mondello et al., "Multidimensional Capillary GC-GC for the Analysis of Real Complex Samples. 3. Enantiomeric Distribution of Monoterpene Hydrocarbons and Monoterpene Alcohols of Mandarin Oils," 46(1) J Agric. Food Chem. 54-61 (Jan. 19, 1998).

[6] World Health Organization, 56 IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 135-162 (1993).

[7] Moyotama et al., Patent Application Laid-Open Disclosure S57-42616, published Mar. 10, 1982.

[8] Exhibit L filed with the Request for Reexamination.

and IARC (Exhibit D). RAN 12.

5. Claims 2, 16, and 17 under 35 U.S.C. § 103(a) as obvious in view of Khan '786, Nazzal, and Chopra[9] as evidenced by Fenaroli, Duetz (Exhibit B), Mondello (Exhibit C), and IARC (Exhibit D). RAN 15.

Background

The '583 patent teaches that CoQ-10 (coenzyme Q10),[10] commonly known as ubiquinone, is essential for the production of cellular energy. '583 patent, col. 1, ll. 20-22. The '583 patent describes clinical studies in which Q10 supplementation has been found to support blood pressure and cholesterol levels and improve cardiovascular health. *Id.* at col. 1, ll. 44–48. The '583 patent discloses that Q10 is sparingly soluble in most hydrophilic solvents, such as water, which limits its bioavailability. *Id.* at col. 1, ll. 51–56. The '583 patent characterized the invention as "the surprising discovery that ubiquinone (CoQ-10) can be readily dissolved in varying concentrations in monoterpenes." *Id.* at col. 3, ll. 55-57. This approach satisfied the "need in the art for an improved methodology to deliver increased amount of bioavailable CoQ-10 to an individual in need thereof." *Id.* at col. 1, ll. 60–62. The monoterpenes described in the '583 patent include limonene and carvone. *Id.* at col. 4, ll. 58-62.

CLAIM INTERPRETATION

Claim 1 is directed to a "solubilized co-enzyme Q-10 composition." The

[9] U.S. Patent No. 6,740,338 B1, issued on May 25, 2004, to Raj K. Chopra.
[10] For brevity, we use the abbreviation "Q10" throughout this decision. The Examiner also used the abbreviation "Q-10."

claim recites that the composition comprises "a sufficient quantity of d-limonene suitable to solubilize said coenzyme Q-10. The '583 patent teaches that the "phrase 'sufficient quantity of a monoterpene suitable to solubilize coenzyme Q-10' is therefore intended to mean that that amount of a monoterpene that will dissolve CoQ-10 under a given set of conditions, generally, those at ambient temperature." '583 patent, col. 4, ll. 21–25. In this case, the monoterpene is limonene. We therefore interpret the term "solubilize" as it is used in the claim means "dissolve."

2. ANTICIPATION REJECTION BY NAZZAL

Rejection

The Examiner found that Nazzal describes a composition comprising "solubilized coenzyme Q10 in lemon oil, which generally comprises approximately 90% or more d-limonene, as evidenced by Fenaroli (page 389) with Exhibit B (page 2829), Exhibit C (page 59, Table 6), Exhibit D (page 135)." RAN 7. The Examiner found that Nazzal "shows that as the relative amount of lemon oil is increased, the temperature at which the coenzyme Q10 melts and solubilizes in solution can be reduced from about 51°C (melting temperature of coenzyme Q10) to below room temperature (Fig. 4; col. 5, line 45 to col. 6, line 40)." *Id.*

The Examiner acknowledged that Nazzal describes melting the Q10 in lemon oil, but stated that the recited language in the claims does "not exclude solubilizing or dissolving via melting." *Id.* at 17. The Examiner further stated that Patent Owner has not demonstrated "any difference between the prior art binary mixtures of coenzyme Q10 and lemon oil (d-limonene) and the claimed composition comprising coenzyme Q10 and d-limonene." *Id.* at 18.

The following findings of fact ("FF") are pertinent to the Examiner's determination that Nazzal anticipates the claimed subject matter:

FF1. Nazzal teaches that Q10 and a volatile essential oil (L-menthol, spearmint oil, lemon oil and anise oil) were mixed and then heated to different temperatures to determine the temperature at which the mixture melted. Nazzal 112–115; Figures 4.8–4.12.

FF2. Specifically, Fig. 4.13 of Nazzal shows a temperature range, of about 15°C to about 50°C, over which Q10 was melted with the essential oil using different weight/weight ratios of Q10 to essential oil.

FF3. Figs. 4.8–4.12 of Nazzal show the differential scanning calorimetry (DSC) thermograms of various volatile essential oils and Q10. The data in these figures was used to construct the graph in Fig. 4.13. *Id.* at 112-115. Fig. 4.11 shows the DSC thermogram for Q10 and lemon. Each point in Fig. 4.13 was determined from a DSC thermogram of Q10 and a specific amount of the essential oil.

FF4. The data in Figs. 4.8 to 4.13 clearly shows that the binary combination of Q10 and essential oil (such as lemon oil) formed a melted composition at a specific temperature for a specific ratio of Q10 to oil.

Issue

The issue in this rejection is whether Nazzal's teaching of a melted composition of Q10 and lemon oil anticipates the claimed "solubilized coenzyme Q-10 composition" which comprises Q10 and "a sufficient quantity of d-limonene suitable to solubilize" the Q10. In other words, does melting Q10 in lemon oil (FF1) result in a composition in which Q10 is solubilized, namely dissolved, in the d-limonene?

Since Nazzal does not expressly teach that the Q10 dissolves in d-limonene, the rejection is based on "inherency," that is, while Nazzal does not describe its composition with the same terms recited in the claim, the claimed composition would be a necessary result of making the composition described in Nazzal.

> [A] prior art reference may anticipate when the claim limitation or limitations not expressly found in that reference are nonetheless inherent to it. . . . Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art.

MEHL/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1365 (Fed. Cir. 1999).

Anticipation does not require the skilled worker to have recognized that the Q10 was dissolved in the d-limonene as long as it would happen each time the directions in Nazzal were followed.

Discussion

Patent Owner contends that Nazzal does not anticipate the claimed "solubilized coenzyme Q-10 composition" comprising d-limonene because Nazzal "does not disclose that CoQ-10 can be dissolved in lemon oil, and instead teaches melting point reduction as an alternative way to liquefy CoQ-10 precisely because it is difficult to dissolve." Appeal Br. 23. Patent Owner argues that Nazzal does not provide "a solution in which coenzyme Q-10 is dissolved," but rather "states that the 'poor water solubility' of coQ-10 is overcome by reducing the melting point of coQ10, so that it becomes a liquid at or below 30°C." *Id.* To support this position, Patent Owner cites the following disclosure from Nazzal:

FF5

> Due to the limited solubility of CoQ-10 in fixed oils and triglycerides, the melting point depression method using essential oils provides an attractive alternative for the preparation of an emulsified formulation.

Nazzal 115.

Patent Owner further argues that Nazzal "distinguishes between melting and dissolving and states that melting is an attractive alternative to traditional approaches that unsuccessfully sought to dissolve coenzyme Q-10." Appeal Br. 24. To support this position, Patent Owner points to the following disclosure in Nazzal:

FF6

> In a eutectic-based self-nanoemulsifying, the melting point depression method allows the oil phase containing the drug itself to melt at body temperature from its semisolid consistency and disperse to form emulsion droplets in nanometer size range.

Id. at 112.

Patent Owner also cites a District Court Order ("Dist. Ct. Order") in an infringement action in the United States District Court Central District of California (CV 10-8301 PSG) asserting Khan '786 against, *inter alia*, Patent Owner. *See* 2012 WL 3186576 (2012). In the District Court Order, the court rejected the position that melting as used in Khan '786 is "synonymous" with dissolving. Dist. Ct. Order 11. The District Court decision was affirmed by the Federal Circuit under Fed. Cir. R.36 (Oct. 8, 2014, 2014-1020, -1033, -1039).

Nazzal is the Ph.D. dissertation of one of the co-inventors of Khan '786. According to Patent Owner, Nazzal's dissertation "resulted in the Khan patent application." Appeal Br. 21. Patent Owner states the "relevant disclosure of

Nazzal is the same as the disclosure in the Khan patent, and thus suffers from the same disclosure deficiencies as Khan." *Id.* Patent Owner did not distinguish between the disclosure in Khan '786 and Nazzal, but rather appears to have made the same arguments for both publications. *Id.* at 21-31. Consequently, we find that the District Court's findings regarding Khan '786 are applicable to Nazzal.

The Order construed "melting" to be "'a phase transition from solid to liquid' through the application of heat." Dist. Ct. Order 10. The district court, however, did not provide a definition of "dissolve."

FF7. Because no definition is of record for us to consider, we have consulted a general chemistry textbook to determine the meaning of "dissolve" and "dissolving." "Dissolve" is defined in the following manner: "When a solute dissolves, the individual particles of solute become surrounded by solvent particles" to produce a "solution."[11] A "solution" is a homogeneous combination of solute and solvent particles. *General Chemistry - Principles, Patterns, and Applications*[12] 1172 (hereinafter, "*General Chemistry*.") See also RAN 4 ("A true solution is a homogeneous mixture of two or more substances.")

The Examiner found that melting is "closely related" to dissolving because both involve energy changes. RAN 18. The Examiner did not cite support for this

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[11] *The Basics of General, Organic, and Biological Chemistry* (2011), v. 1.0, Ball, David, W., Hill, John W., and Scott, Rhonda, J., Section 9.3, "The Dissolution Process," Flat World Education, Inc. (2015). Accessed at http://catalog.flatworldknowledge.com/bookhub/reader/2547?e=gob-ch09_s03 (Dec. 11, 2015). Hereinafter, "*Chemistry Basics*."

[12] Averill B. and Eldredge, P. (2011) http://www.saylor.org/site/textbooks/General%20Chemistry%20Principles,%20Patterns,%20and%20Applications.pdf

statement apparently because the statement reflects well known principles in chemistry. The Examiner's finding is factually supported as follows:

> FF8
>
> Physical changes, such as melting or vaporization, and chemical reactions, in which one substance is converted to another, are accompanied by changes in enthalpy [energy change]. Two other kinds of changes that are accompanied by changes in enthalpy are the dissolution of solids and the dilution of concentrated solutions.

General Chemistry 444.

FF9. When a solute dissolves in a solvent, "energy is required to overcome the intermolecular interactions in a solute." *Id.* at 1173. Similarly, the "melting point" is when the ions or atoms in a solid have enough energy to overcome the intermolecular attractive forces which hold them together. *Id.* at 684, 795, 981, 985, 1029, 1071.

Thus, as found by the Examiner, "melting" is closely related to "dissolving" because of the change in energy when the intermolecular interactions between the atoms in the solid are overcome as the solid melts or as the solute particles in the solid dissolve in the solvent. A key difference between melting and dissolving is that melting involves only a change in state of the solid into a liquid when the intermolecular forces that hold the atoms in the solid together are overcome, while dissolving involves overcoming the attractive forces between the atoms in the solid and mingling the solid atoms homogenously with solvent particles. When a solid dissolves in the solvent, it could just as well be said that it "melts" because, as with the melting process, the intermolecular forces that hold the solid atoms together are overcome allowing it to become dispersed in solvent.

The next question is whether the Q10 forms a solution when it melts in the presence of the lemon oil. The Examiner's position is that it does because of the close relationship between melting and dissolving, i.e., melting results in overcoming the intermolecular interactions of the atoms in the solid, permitting them to disperse within the lemon oil solvent as would happen when the intermolecular forces are overcome in dissolving. The Examiner's reasoning is supported by Dr. Nazzal's testimony in his declaration in which he describes his work reported in the Khan '786 patent. RAN 22–23. Dr. Nazzal testified (emphasis added):

> 4. The '786 Patent [Khan] describes and teaches the surprising and unexpected discovery that a sufficient amount of volatile essential oil reduces the melting point of CoQ10 to 37°C or below to thereby liquefy and solubilize the CoQ10 at or below body temperature.
>
> 5. At the time of our invention, I was not aware of any CoQ10 formulation in commercial use or in the literature that contained CoQ10 that was solubilized with a volatile essential oil or solubilized with a sufficient amount of a volatile essential oil that would reduce CoQ10's melting temperature.

Dr. Nazzal thus explains when the Q10 is melted to a liquid it is "solubilized," namely dissolved in the essential oil (*see* "Claim Interpretation" above finding that solubilize means dissolve).

In sum, a preponderance of the evidence supports the conclusion that when the Q10 and lemon oil form a mixture upon heating (FF1–FF4), the Q10 melts and dissolves in the lemon oil.

Patent Owner's argument that Khan '786's use of the term "solubilize" is not the same as "dissolve" is unavailing. Appeal Br. 12. Patent Owner contends that Khan '786 and Nazzal distinguish between "dissolve" and "solubilize."

Rebuttal Br. 2. Specifically, Patent Owner argues that "solubilize" is used in Khan '786 in the context of utilizing surfactants. *Id.* at 3.

In our opinion, it is not clear cut that Khan '786 and Nazzal use the terms "dissolve" and "solubilize" in all instances to mean different chemical processes. For example, in the passage reproduced below, Nazzal refers to dissolving Q10 in acetone and then to "solubilized" Q10 in acetone, suggesting that in this instance the terms are used in the same way.

> To eliminate the effect of temperature on the integrity CoQ_{10}, stock solution (0.1 mg ml^{-1}, 0.1% Cremophor EL) was prepared by dissolving 100 mg of CoQ_{10} in 3 ml of acetone. One gram of Cremophor EL was added and mixed with the solution and subsequently diluted to 1 liter with distilled water. Similarly, to evaluate the effect of Cremophor EL concentration on CoQ_{10} analysis, a stock solution (0.1 mg ml^{-1}, 1% Cremophor EL) was prepared by mixing solubilized CoQ10 in acetone with 10 grams of Cremophor EL. Assay validation was performed as described above.

Nazzal 67 (emphasis added).

Although Patent Owner attempts to establish that "solubilize" requires the presence of solubilizing agents (Appeal Br. 12–13), Dr. Nazzal does not refer to the presence of a solubilizing agent in his statements in paragraphs 4 and 5 of his declaration. Moreover, Patent Owner has not explained why "solubilizing" a drug with a "solubilizing agent" would not result in the drug being dissolved in the solubilizing agent. Patent Owner has largely focused on word definitions, and perhaps the imprecise and loose use of the word, without explaining the actual chemical processes that occur when a compound is dissolved or solubilized.

Nonetheless, the rejection is based on inherency, and even if Khan '786 and Nazzal use the terms "dissolve" and "solubilize" to mean different chemical processes, the issue is not whether the two publications described Q10 dissolved in

lemon oil, and its main constituent d-limonene, but whether, when Khan '786 and Nazzal are followed, would the necessary result be Q10 dissolved in d-limonene.

Patent Owner also contends that the "mechanism" by which "one gets to a liquid solution . . . cannot be ignored." Appeal Br. 13. The Examiner has not ignored this step. As explained, when heat is applied to the binary combination of lemon oil and Q10, the attractive forces in the atoms are overcome in the Q10 and it dissolves in the lemon oil. Patent Owner denies that dissolving occurs, but has offered no alternative explanation as to what happens to the atoms of Q10 and lemon oil upon the application of heat.

The District Court Order is not inconsistent with the conclusion that the Q10 dissolves in the lemon oil. The District Court distinguished melting from dissolving, a finding that does not exclude there from being similarities between the two processes as discussed above. Moreover, the District Court in the Order acknowledged that the melting point reduction process in Khan '786 in which a eutectic was formed resulted in the Q10 dissolved in lemon oil: "The fact that the melting point reduction is used as a means to solubilize or dissolve and as a basis for distinguishing traditional methods indicates that melting is distinct from dissolving or solubilizing." Dist. Ct. Order 13 (emphasis added). In other words, while the District Court recognized that the "melting point reduction" method is different from dissolving because a reduction in melting temperature is observed in the former and results in "a change in the physical properties" of Q10, it specifically stated the melting point reduction method was a "means to solubilize or dissolve" the Q10. *Id.* The mechanisms may be different, but it is the result which is claimed, not the mechanism, which is relevant to the claims at issue, as there is no temperature limitation set forth in the claims.

d-limonene

FF10. The Examiner found that lemon oil contains 90% or more limonene (citing Fenaroli on page 389), which is mostly d-limonene (Exhibits B-F).[13] RAN 9.

FF11. The Examiner further found that the "limonene in lemon oil contains 98.1 % or 98–100% d-limonene (Exhibit C, page 59, Table 6; Exhibit D, page 135), and d-limonene is the main constituent of orange and lemon peel oil in the amount of 92-96% (Exhibit B, page 2829)." *Id.* at 24. The Examiner's findings regarding these publications are factually supported.

Based on these values, the Examiner found that the binary composition of Q10 and lemon oil as shown in Nazzal's Fig. 4.13, contains "about 36%, 45% and 54% by weight d-limonene (in 40%, 50% and 60% by weight lemon oil) in a mixture with 60%, 50% and 40% by weight of coenzyme Q10 respectively." *Id.* The Examiner concluded that in the binary composition "coenzyme Q10 melts and solubilizes at about 33°C, 26°C and 24°C respectively (Fig. 4), indicating that d-limonene (lemon oil) is suitable for dissolving coenzyme Q10 at ambient temperature or below." *Id.*

Patent Owner disputes the Examiner's finding that lemon oil is always necessarily[14] d-limonene or 90% d-limonene, citing the Lota and Steuer publications as evidence. Appeal Br. 15-16. Patent Owner states:

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[13] We have not considered Exhibits E and F.

[14] "[A] prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." *SmithKline Beecham Corp. v. Apotex Corp.*,

> Patent Owner has submitted evidence that the amount of limonene in lemon oil is less than 40%. See Lota at 797, Table 1 (Ex. V). Accordingly, Exhibits B, C and D, in view of Lota and Steuer, do not meet the Office's burden to show anticipation by inherency; they do not "make clear" that lemon oil is always "necessarily" d-limonene or 90% d-limonene

Id. at 16.

While we have concluded that Q10 dissolves in lemon oil when melted, the claim requires that there is a "sufficient quantity of d-limonene suitable to solubilize" the Q10 "thereby providing a solution in which the coenzyme Q-10 remains solubilized." In other words, even if the Q10 is dissolved in the lemon oil, the claim limitation requires that Q10 be dissolved in the d-limonene present in the lemon oil. The Examiner's reasoning for finding that it is the d-limonene that dissolves the Q10 appears to be based on the fact that d-limonene is the main constituent of lemon oil. Specifically, Exhibits B, C. and D support the Examiner's position that d-limonene is the predominant limonene in lemon oil. FF11. Patent Owner's countervailing evidence is that the amount of *limonene* in lemon oil can be less than 90%, depending on the source. However, we have not been pointed to evidence in these two publications (Lota and Steuer) that the d-limonene is not the main component of the limonene.

Even if it true that the content of limonene is than the 90% value relied upon by the Examiner, this does not answer the *issue* in this rejection, i.e., whether the d-limonene in Nazzal's lemon oil dissolves the Q10 when the lemon oil and Q10 are melted together. Thus, even if the amount of d-limonene present in the lemon

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403 F.3d 1331, 1343 (Fed. Cir. 2005) (citing *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991)).

oil/Q10 mixture described in Nazzal is less than the lower limit of 36% by weight calculated by the Examiner (RAN 24), there still must be evidence that such lower amounts would or would not dissolve Q10.

The Examiner had basis to find that the Q10 dissolves in the d-limonene because, as discussed above, the Q10 dissolves in the lemon oil and a significant amount of d- limonene is present in the lemon oil. Patent Owner argues about the content of limonene in lemon oil, but fails to provide evidence that, if the particular species or strain which is said to contain less limonene than the 90% value assumed by the Examiner had been used in Nazzal,[15] the amounts of d-limonene would have been insufficient to dissolve the Q10.

In our opinion, this controversy about the amounts of limonene and d-limonene in lemon oil that has occupied the Examiner, Patent Owner, and Requester begs the question of how much d-limonene constitutes "a sufficient quantity of d-limonene suitable to solubilize . . . coenzyme Q-10." On this pivotal question, the evidence is that 1) lemon oil solubilizes and dissolves Q10, and 2) d-limonene is principal component of it, giving the Examiner reasonable factual basis[16] to conclude that even lemon oils with less than 90% limonene would have sufficient d-limonene present to dissolve Q10.

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[15] Lemon peel oils: "Limonene was always the main constituent (38.1-95.8%) of all oils." Lota, page 799.

[16] Whether the rejection is based on "inherency" under 35 U.S.C. § 102, on 'prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products." *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) (footnotes omitted).

The lower value of 38.1% identified in one species in Lota (Table 1, "Bor") is still about a third of the higher values: indeed, there is no evidence that this species of lemon oil peel was available to Nazzal.

Under *In re Best*, 562 F.2d 1252 (CCPA 1977), Patent Owner has the burden to prove that the Q10 did not dissolve in the lemon oil of Nazzal.

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.
>
> . . .
>
> Whether the rejection is based on "inherency" under 35 U.S.C. § 102, on "prima facie obviousness" under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products.

Best, 562 F.2d at 1255 (CCPA 1977) (footnote omitted). Patent Owner did not meet this burden.

In sum, the fact that Nazzal's lemon oil was not necessarily 90% limonene or d-limonene (Appeal Br. 13–14) does not undermine the Examiner's finding that Nazzal anticipates the claimed subject matter. In view of this evidence, we conclude that a preponderance of the evidence supports the Examiner's finding that Nazzal necessarily and inherently disclosed Q10 dissolved in d-limonene.

Khan (2004)

Patent Owner argues that a subsequent publication by Khan – Khan (2004)[17]

[17] Anitha Palamakula, Mahmoud Soliman, Indra K. Reddy, and Mansoor A. Khan, "Preparation and *In Vitro* characterization of Self-Nanoemulsified Drug Delivery

– demonstrates that the lemon in Nazzal "was not d-limonene or 90% d-limonene." Appeal Br. 25. According to Patent Owner, Khan (2004) is "a separate study analyzing d-limonene and its ability to reduce the melting point of coenzyme Q10." *Id* at 15. Patent Owner contends:

> If the lemon oil used in Khan and Nazzal were d-limonene or 90% d-limonene, then there would be no reason for Dr. Khan subsequently to study and publish findings on whether d-limonene could be used to reduce the melting point of coenzyme Q10.

Id.

Patent Owner has not provided adequate evidence that subsequent work by Khan's group using d-limonene rather than lemon oil reasonably means that Khan did not believe the lemon oil in the Nazzal was not predominantly d-limonene. Khan (2004) states that the reason for its study was "to study natural substance such as chiral components of essential oils for solubilizing drug compounds." Khan (2004) 74. Khan (2004) further states that limonenes exist in two chiral conformations and the R-(+) form, also known as d-limonene. *Id*. Furthermore, Khan states that that "[r]esearch in the food industry has demonstrated R-(+)-limonene in microemulsions as vehicles to enhance the solubilization of natural food supplements," but acknowledges that the "available literature is scare . .. about using these components to prepare SNEDDS." *Id*. Thus, it appears Khan (2004) reason for studying d-limonene was its interest in chiral component.

Systems of Coenzyme Q10 Using Chiral Essential Oil Components," Pharmaceutical Technology 74–88 (October 2004).

Emulsion

Patent Owner contends that Nazzal does not anticipate the claimed subject matter because "it does not disclose a solution that is not part of an emulsion." Appeal Br. 26. The Examiner has relied upon the binary combination of lemon oil and Q10. FF1–FF4, FF6. There is no persuasive evidence in this record that the melt of Q10 and lemon oil described in findings FF1–FF4 is an emulsion.

Dependent claims

Patent Owner did not provide separate reasons for the patentability of claims 2, 6–10, and 15. Appeal Br. 21. Thus, these claims fall with independent claim 1. 37 C.F.R. § 41.67(c)(vii).

1. ANTICIPATION BASED ON KHAN '786

As stated above, Nazzal is the Ph.D. dissertation of one of the co-inventors of Khan '786. Patent Owner states the "relevant disclosure of Nazzal is the same as the disclosure in the Khan patent, and thus suffers from the same disclosure deficiencies as Khan." Appeal Br. 21. Patent Owner did not distinguish between the disclosure in Khan '786 and Nazzal, but rather appears to have made the same arguments for both publications. *Id.* at 21-31. Thus, we affirm the anticipation of rejection over Khan '786 for the same reasons as those set forth for Nazzal.

3. OBVIOUSNESS BASED ON KHAN '786

The Examiner found that Khan '786 does not describe using d-limonene to dissolve Q10 as required by the claims. RAN 10. However, the Examiner found that Nazzal suggests using d-limonene instead of lemon oil. *Id.* at 11. The Examiner also found that d-limonene is the main constituent of lemon peel oil,

citing Exhibits B–D. *Id.* The Examiner concluded that "would have been obvious for one of ordinary skill in the art to use d-limonene, the major active component of lemon oil, instead of lemon oil as suggested by Nazzal to solubilize coenzyme Q10 and arrive at the composition of claim 1, and with a reasonable expectation of success." The Examiner provided fact-based reasons as to why dependent claims 2, 4, 6-10, and 15 would have been obvious to one of ordinary skill in the art. *Id.* at 11–12. Patent Owner's arguments regarding Khan '786 are the same arguments we found unpersuasive for the anticipation rejection based on Khan '786. Appeal Br. 28. Patent Owner contends that the Examiner erred (*id.*) in stating that "Nazzal . . . specifically teaches that instead of using lemon oil, its major chemical component, limonene, can be used to achieve the melting point reduction of coenzyme Q10 (page 246). RAN 11."

We thus turn to Nazzal's disclosure. Under the section titled "Recommendations for future studies," Nazzal stated "Chemical components of essential oils such as limonene, menthone, and carvone can be evaluated for their potency in exerting a eutectic effect." Nazzal 246. Nazzal therefore suggests evaluating limonene to determine whether it can be used to achieve the melting point reduction of coenzyme Q10, but does not expressly say that it "can be used" for such purpose as found by the Examiner. Because the Examiner erred in making this statement, and based the rejection on this erroneous finding, we are compelled to reverse the rejection.

4. REJECTION BASED ON MOTOYAMA

The Examiner found that Motoyama describes Q10 dissolved in carvone, which includes l-carvone derived from spearmint oil and peppermint oil and d-

carvone from caraway seed oil. RAN 12. The Examiner stated that it would have been obvious to have utilized d-limonene instead of a carvone-containing oil because both were known to be effective in solubilizing Q10 as demonstrated by Khan '786. *Id.* at 13.

In this case, we find there is adequate evidence that one of ordinary skill in the art would have had reason to use d-limonene to dissolve Q10 with a reasonable expectation of success.[18] The following facts are pertinent to this determination:

FF12. Motoyama teaches that carvone, a monoterpene ('583 patent, col. 4, ll. 58–62), dissolves Q10. Motoyama 5 (col. 2) ("[C]arvone is a particularly preferred oil due to good solubility for ubiquinone and the property of dissolving an equal weight of ubiquinone at room temperature.").

FF13. Motoyama teaches that "refined oils that contain carvone (such as peppermint oil, spearmint oil, or the like) are preferred for the present invention due to the ability to dissolve ubiquinone well." *Id.*

FF14. Khan '786 discloses that essential oils, such as menthol, peppermint oil, spearmint oil, and lemon oil lower the melting temperature of Q10, making them useful in a delivery system for Q10. Khan '786, col. 6, ll. 24–27, col. 6, l. 65 to col. 7, l. 35.

FF15. D-limonene is a monoterpene ('586 patent, col. 4, ll. 58–62) and the main constituent of lemon peel oil (Duetz 2829 (Exhibit B)("D-Limonene is the

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[18] To decide whether a composition would have been obvious in light of the prior art, it must be determined whether, at the time of invention, "a person of ordinary skill in the art would have had reason to attempt to make the . . . [composition], . . . and would have had a reasonable expectation of success in doing so." *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007).

main constituent of orange and lemon peel oil (92 to 96%) . . ."); (IARC 135 (Exhibit D) ("the d form [of limonene] comprises 98-100% of the limonene in most citrus oils (family Rustaceae)")); Mondello, Table 6 (Exhibit C)("limonene (4R)(+) 98.1"))

FF16. Nazzal recommended for future studies that "[c]hemical components of essential oils such as limonene, menthone, and carvone can be evaluated for their potency in exerting a eutectic effect." Nazzal 246.

Discussion

A preponderance of the evidence supports the Examiner's determination that one of ordinary skill in the art would have had reason to utilize d-limonene to dissolve Q10.

First, Motoyama teaches that another monoterpene dissolves Q10 and teaches that some of the same oils (spearmint, peppermint) described as effective by Khan '786 are preferred for their ability to dissolve Q10.[19] FF12–FF14. Because of the overlap in disclosure of essential oils between Motoyama and Khan '786, one of ordinary skill in the art would have had reason to have used Khan '786's oils in Motoyama's method in amounts sufficient to dissolve Q10, with a reasonable expectation that they would work. That is, since Motoyama teaches that spearmint and peppermint oil dissolve Q10, and Khan '786 teaches using these

[19] The '583 patent described its invention as "the surprising discovery that ubiquinone (CoQ-10) can be readily dissolved in varying concentrations in monoterpenes." '583 patent, col. 3, ll. 55-57. However, it appears that Motoyama had at least already discovered the Q10 could dissolve in the monoterpene carvone, providing the same solution to the problem identified in the '583 patent of delivering increased amounts of bioavailable Q10. *Id.* at col. 1, ll. 55–62.

same oils in conjunction with Q10, the skilled worker would have had basis to believe that Khan '786's lemon oil, when used in a sufficient amount, would work in Motoyama's method to *dissolve* Q10.

Second, while Khan '786 does not identify d-limonene as a component of lemon oil, d-limonene is a main constituent of lemon peel oil. FF11.

The skilled worker would have had reason to use d-limonene in Motoyama's method because it is a monoterpene like Motoyama's carvone (FF13, FF15), and Nazzal explicitly suggested d-limonene for future studies (FF16). Nazzal also suggested evaluating carvone for its potency in exerting a eutectic effect when combined with Q10 (FF16), further indicating the interchangeability of carvone and d-limonene, or at least the reasonable belief that they would have similar properties.

Patent Owner argues that Khan '786 does not teach that lemon oil or d-limonene can be used to dissolve Q10. Appeal Br. 31–32. Patent Owner argues that, "[o]n the contrary, Khan [] teach[es] melting point reduction as an alternative . . . approach to liquefying CoQ-10, precisely because it is difficult to dissolve." *Id.* at 32. Furthermore, Patent Owner contends there would be no reasonable expectation of success since Khan '786 is "directed to reducing the melting point of coenzyme Q-10, not dissolving it." *Id.* Patent Owner states that Khan '786 "teaches away" from utilizing d-limonene to dissolve Q10 because Khan '786 uses "melting point reduction because coenzyme Q-10 is difficult to dissolve." *Id.* at 33.

Patent Owner argues that Khan '786's subsequent publication, Khan (2004), investigating d-limonene is evidence of nonobviousness:

> If it was obvious at the time of the '583 patent application, that

> d-limonene could be used to reduce the melting point of CoQ-10, then Khan himself [in Khan 2004], would not have been investigating subsequently whether d-limonene could be so-used. Similarly, if it was obvious that d-limonene could be substituted for Motoyama's carvone, then Khan would not have been teaching melting point reduction as an alternative to address the fact that CoQ-10 is difficult to dissolve.

Id. at 34.

Patent Owner's arguments are not supported by adequate evidence of record. Even if the disclosed mechanisms are different – where Khan '786 describes "melting" Q10 and Motoyama describes "dissolving" Q10 – Motoyama specifically teaches that spearmint and peppermint oils dissolve Q10 (FF13) and these same oils are described by Khan '786 as depressing the melting temperature of Q10 (FF14). Consequently, in view of Motoyama, the skilled worker would have recognized that certain oils that depress the melting temperature of Q10 also dissolve it when an adequate amount of such oil is used for a given amount of Q10. Based on this, the skilled worker would have had reason to use lemon oil and its main constituent d-limonene in Motoyama's method with a reasonable expectation that it would work because other oils shown to depress the melting temperature of Q10 were shown in Motoyama's experiments to dissolve it.

We do not agree that that Khan '786's later experiments with d-limonene is evidence of nonobviousness. Nazzal expressly suggested evaluating d-limonene (FF16), providing explicit evidence that one of ordinary skill in the art had reason to use it at the time of the invention. In view of this explicit suggestion in Nazzal, one of ordinary skill in the art would had reason to use d-limonene in Motoyama's method, as well, since d-limonene is a monoterpene like carvone which had been shown to dissolve Q10. Indeed, it was later shown by Khan (2004) that

d-limonene dissolves Q10. Khan (2004) states "CoQ is fairly soluble in monoterpenes, R-limonene [d-limonene] (571.6 ± 5.03 mg/mL)." Khan (2004) 78.

As held in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421(2007):

> 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.

There is no persuasive evidence of record that one of ordinary skill in the art would have had "to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988); *Bayer Schering Pharma AG v. Barr Labs., Inc.*, 575 F.3d 1341, 1347 (Fed. Cir. 2009).

For the foregoing reasons, we conclude that a preponderance of the evidence supports the Examiner's determination that claim 1 is obvious in view of Motoyama, Khan '786, Fenaroli, Exhibits B, C, and D, and Nazzal. Claims 2, 4, 6-10, 12, 13, and 15 were not argued separately and thus fall with claim 1 and for the reasons set forth by the Examiner.

5. OBVIOUSNESS BASED ON KHAN '786 AND CHOPRA

Dependent claims 2, 16, and 17 are directed to Q10 which is oxidized, reduced, or semi-reduced (claim 2), reduced (claim 16), and semi-reduced (claim 17). The Examiner found that it was known at the time of the invention that Q10

could be in the form of the three recited redox states. RAN 16. The Examiner found that Chopra teaches that reduced Q10 is useful for treating heart ailments and diseases. *Id.* The Examiner concluded that it would have been obvious to have used "the reduced form or the semi-reduced form of coenzyme Q10 instead of the oxidized co-enzyme Q10 of Khan or Nazzal to arrive at the claimed invention. There would have been a reasonable expectation of success, especially in view of the teaching of Chopra." *Id.*

Patent Owner challenged the rejection based on the same arguments against Khan '786. Appeal Br. 34. As we found these arguments unavailing (Ground 1 above), we affirm the rejection of these claims.

TIME PERIOD FOR RESPONSE

In accordance with 37 C.F.R. § 41.79(a)(1), the "[p]arties to the appeal may file a request for rehearing of the decision within one month of the date of: . . . [t]he original decision of the Board under § 41.77(a)." A request for rehearing must be in compliance with 37 C.F.R. § 41.79(b). Comments in opposition to the request and additional requests for rehearing must be in accordance with 37 C.F.R. § 41.79(c), (d), respectively. Under 37 C.F.R. § 41.79(e), the times for requesting rehearing under paragraph (a) of this section, for requesting further rehearing under paragraph (d) of this section, and for submitting comments under paragraph (c) of this section may not be extended.

An appeal to the United States Court of Appeals for the Federal Circuit under 35 U.S.C. §§ 141-144 and 315 and 37 C.F.R. § 1.983 for an *inter partes* reexamination proceeding "commenced" on or after November 2, 2002 may not be taken "until all parties' rights to request rehearing have been exhausted, at which

time the decision of the Board is final and appealable by any party to the appeal to the Board." 37 C.F.R. § 41.81. *See also* MPEP § 2682 (8th ed., Rev. 7, July 2008).

In the event neither party files a request for rehearing within the time provided in 37 C.F.R. § 41.79, and this decision becomes final and appealable under 37 C.F.R. § 41.81, a party seeking judicial review must timely serve notice on the Director of the United States Patent and Trademark Office. *See* 37 C.F.R. §§ 90.1 and 1.983.

AFFIRMED

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Patent 8,105,583 B2

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EXHIBIT A