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KILPATRICK TOWNSEND & STOCKTON LLP
1100 PEACHTREE STREET
SUITE 2800
ATLANTA, GA 30309

EXAMINER	
IVANOVA, SVETLANA M	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
04/22/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipefiling@kilpatricktownsend.com
jlhice@kilpatrick.foundationip.com
mcollins@kilpatricktownsend.com

Office Action Summary	Application No. 13/582,133	Applicant(s) CLEMENTS ET AL.	
	Examiner SVETLANA M. IVANOVA	Art Unit 1627	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/24/2014*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1-4 and 6-8* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-4 and 6-8* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.

The present application is being examined under the pre-AIA first to invent provisions.

Response to Arguments

Applicant's response from 1/21/2014 is acknowledged.

Claim rejections- 35 USC 102(b)

-Azam

-Va gasena

-Thiruvalluvar gnana vettian

-Haque

Applicant has provided a response to the rejections with respect to the claims as currently amended. As the Examiner has not had a chance to address these amended claims, a modified rejection under 35 USC 103(a) has been made below, which now renders Applicant's arguments moot.

Claim rejections- 35 USC 103(a)

-Haque, further in view of Banerjee

-Haque, further in view of Azam, Va gasena, Thiruvalluvar gnana vettian

Applicant has provided a response to the rejections with respect to the claims as currently amended. As the Examiner has not had a chance to address these amended

claims, a modified rejection under 35 USC 103(a) has been made below, which now renders Applicant's arguments moot.

Claims 1-4 and 6-8 are pending, and have been examined herewith.

Claim Rejections - 35 USC § 103

The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, 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 said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 6-8 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over US 6,406,706 to Haque *et al.* ("Haque", of record), further in view of and Piggott *et al.*, Western Austrian Sandalwood Oil" Extraction by Different Techniques and Variations of the Major Components in Different Sections of a Single Tree, Flavour and Fragrance Journal, Vol. 12, 43-56 (1997) ("Piggott"), and Banerjee *et al.*, Modulatory influence of sandalwood oil on mouse hepatic glutathione S-transferase activity and acid soluble sulphydryl level, Cancer Letters, 68 (1993) 105-109 ("Banerjee", of record)-- alone, or in combination with either or all of-- Ikseer Azam, Vol. IV 19th century, Matba Nizami, Kanpur, 1872 AD, p. 309, TKDL identifier BA4/1854C ("Azam", of record), Va gasena, 12th Century- commentator Shaligram Vaisya, Edited Shankar lalji Jain;

Khemraj Shrikrishna Das Prakashan, Bombay, Edn. 1996, page 811, TKDL identifier AK11/3505 ("Va gasena", of record) and Thiruvalluvar gnana vettian, 10-15th Century A.D., Ed: Mangadu Vadivel Mudalia, Pub: Parthina Nayakar & sons, Thirumagal vilakku press, Chennai, Page 272-278, TKDL identifier GP11/20 ("Thiruvalluvar gnana vettian", of record).

Haque discloses the use of α- and β-santalols- found to be the therapeutic ingredients of sandalwood oil- in a composition for the treatment of HPV-induced tumors, such as cancer of the skin and cervix- i.e. for the treatment with an effective amount of both skin and non-skin cancer in a human. (Abstract; col. 1, ll. 22-23; claims 1 and 5). The α- and β-santalols are obtained from at least one Santalum species selected from the group consisting of S. album, S. yasi, S. papuanum and S. spicatum. (claim 3). The α- and β-santalols are formulated for topical application, e.g. as soap with other excipients, i.e. with pharmaceutically acceptable excipients. (col. 3, l. 56- col. 4, l. 4).

Hague discloses treatment with sandalwood oil of skin and cervical cancer, but does not explicitly disclose treatment of other specific cancers, per Applicant's claims 6-8.

Banerjee discloses that sandalwood oil from S. album, given by oral administration (5 μl or 15 μl for 10 and 20 days) to mice, shows an enhancement of glutathione S-transferase (GST) activity and of acid-soluble sulfhydryl (SH) levels, which is suggestive of a possible chemopreventive action of sandalwood oil on carcinogenesis. (Abstract). Measurements in the study are done based on extracts

from liver tissue. (p. 106). With respect to doses, the study demonstrated that this oral gavage treatment led to significantly higher SH content in animals treated with both dose levels for 10 days, whereas the increase seen with treatment at 15 μl was significant in only the 10-day treatment group. (p. 108, col. 1).

Thus, Banerjee alone discloses an additional specific cancer, per Applicant's claims 6-8. The following prior art references- Azam, Va gasena and Thiruvalluvar gnana vettian- whether applied separately, or in combination with Banerjee, further affirm this conclusion. They all show that sandalwood oil has been used for hundreds of years in India for treatment of cancer broadly, and not just of the particular cancers disclosed in Hague.

Azam discloses a therapeutic compound formulation comprising *inter alia* sandalwood from S. album (which encompasses sandalwood oil) together with other pharmaceutically acceptable excipients, which is formulated as oil and is useful in the treatment of cancer. Administration is local as liniment. Azam discloses treatment of cancer broadly. A person of skill in the art would understand this to encompass the particular cancers of Applicant's claims 6-8.

Va gasena discloses a therapeutic compound formulation comprising *inter alia* sandalwood heartwood from S. album (which encompasses sandalwood oil) together with other pharmaceutically acceptable excipients, which is formulated as medicated oil and is useful in tumor treatment. Administration is via the nasal route, in a dose as directed by a physician. Va gasena discloses treatment of cancer broadly. A person of

skill in the art would understand this to encompass the particular cancers of Applicant's claims 6-8.

Thiruvalluvar gnana vettian discloses a therapeutic compound formulation comprising *inter alia* sandalwood seed from S. album (which encompasses sandalwood oil) together with other pharmaceutically acceptable excipients, which is formulated as medicated oil and is useful in tumor treatment. The administration is local, as directed by a physician. Thiruvalluvar gnana vettian discloses treatment of cancer broadly. A person of skill in the art would understand this to encompass the particular cancers of Applicant's claims 6-8.

Haque and Banerjee both disclose isolated sandalwood oil, or some of its active ingredients, but do not disclose that such sandalwood oil can be either distilled or extracted, per Applicant's claims as amended.

Piggott discloses that steam distillation, solvent extraction, supercritical fluid extraction and liquid CO2 extraction are all techniques for obtaining sandalwood oil from Western Australian Sandalwood (*S. spicatum*). (Abstract). Piggott further discloses that when the essential oil from *S. spicatum* was first investigated in the 1920s, it was found that it contained up to 35% of α- and β-santalol, i.e. considerable proportions of farnesol were present. A later examination of steam-distilled oil from the trunkwood showed that sesquiterpene alcohols accounted for more than 90% of the content, with the major components being:

> 2(*E*), 6(*E*)-farnesol (31.6%), *epi*-α-bisabolol (10.7%), (*Z*)-α-santalol (9.1%), (*Z*)-nuciferol (6.5%) and (*Z*)-β-santalol (5.4%).

(p. 43, col. 1 and 2). Per Piggott, this suggested that there are different varieties of sandalwood, and that they might vary in different sections of a single tree. (*Id.*). Therefore, in Piggott the investigators studied extraction by varying: 1) all of the different methods specified above, and 2) selecting different sections of the wood- e.g., branchwood, buttwood. (p. 44, col. 2- p. 45- col. 1). The results showed considerably variance in the extracted ingredients depending on the methods of extractions, and the different sections of wood. (Tables 1, 2 and 3, and discussion pertaining to these tables). *See also* p. 45, col. 2, which provides as follows:

> Also interesting are the percentages of five of the major sesquiterpene components (1–5), *epi*-α-bisabolol (1), (*Z*)-α-santalol (2) 2(*E*),6(*E*)-farnesol (3), (*Z*)-β-santalol (4) and (*Z*)-nuciferol (5), present in each extract. Steam distillation leads to a much greater proportion (54.2%) of these sesquiterpenes than the other extraction techniques (24.4–26.1%), although the relative ratios are similar.

Accordingly, it would have been obvious to a person of skill in the art, based on the combination of Haque, Pigott and Banerjee- alone, or in combination with and either or all of Azam, Va gasena and Thiruvalluvar gnana vettian, to treat different types of cancer with sandalwood oil with a reasonable chance of success. A person of skill in the art would have been motivated to do so as Haque shows sandalwood oil to treat different types of cancer- e.g. of the skin and of the cervix on topical application, and Banerjee further suggests that oral administration of sandalwood oil has a chemopreventative action on carcinogenesis, as exemplified from results obtained from liver tissue (i.e. non-skin related). A person of skill in the art would have been further

motivated to do so as traditional medicine sources from India (Azam, Va gasena and Thiruvalluvar gnana vettian) point to the use of sandalwood for treating cancer broadly, and not just a particular type of cancer. Based on this disclosure, a person of skill in the art would have been motivated to use sandalwood oil for treating a variety of cancers, to include non-skin cancers.

Although both Haque and Banerjee do not explicitly disclose the particular amounts claimed by Applicants, per Applicant's claims as amended, it would have been further obvious to a person of skill in the art to optimize these amounts, in order to arrive at Applicant's claimed range in % (w/w). A person of skill in the art would have been motivated to do so in order to enhance the therapeutic efficacy. Generally, mere optimization of ranges will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "When the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); "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 Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003). It has been held that it is within the skills in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. *In re Boesch*, 205 USPQ 215 (CCPA 1980). MPEP 2114.04. Moreover, motivation to do so is additionally found in Banerjee, which shows a study with optimizing such ranges, as

expressed in μl. A person of skill in the art would have been motivated to estimate such ranges in other units as well (such as claimed by Applicant), guided by the disclosure in Banerjee that not all doses studied were found to be efficacious for the duration of treatment, with the lower dose showing better efficacy. A person of skill in the art would have been further motivated to do so guided by the disclosure in Piggott, which shows that it is essential for distilled or extracted sandalwood oil to determine such therapeutic ranges, as depending on the technique of extraction used, and the portion of wood used, the amounts of the active ingredients in sandalwood vary significantly. Thus, the skilled artisan would have had at its disclosure at the time of the invention multiple sources independently of one another, and complimentary to one another, establishing motivation to optimize the dose range of sandalwood oil in practicing the claimed method.

Other relevant art

The Examiner also notes for the record the following cumulative prior art-references 2, 6-12, 14, 16-22 of Applicant's IDS dated 1/21/2014.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SVETLANA M. IVANOVA whose telephone number is (571)270-3277. The examiner can normally be reached on Mon.-Fri. 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SVETLANA M. IVANOVA/
Examiner, Art Unit 1627