

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing
(day/month/year)

15.04.2020

Applicant's or agent's file reference
P40551WO

IMPORTANT NOTIFICATION

International application No.
PCT/EP2019/052069

International filing date (day/month/year)
29.01.2019

Priority date (day/month/year)
29.01.2018

Applicant
Phytoplant Research S.L.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international
preliminary examining authority:



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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P40551WO	FOR FURTHER ACTION		See Form PCT/IPEA416
International application No. PCT/EP2019/052069	International filing date (day/month/year) 29.01.2019	Priority date (day/month/year) 29.01.2018	
International Patent Classification (IPC) or national classification and IPC INV. C07C37/72			
Applicant Phytoplant Research S.L.			
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☒ (sent to the applicant and to the International Bureau) a total of <u>7</u> sheets, as follows: ☒ sheets of the description, claims and/or drawings which have been amended and/or sheets containing rectifications authorized by this Authority, unless those sheets were superseded or cancelled, and any accompanying letters (see Rules 46.5, 66.8, 70.16, 91.2, and Section 607 of the Administrative Instructions). ☐ sheets containing rectifications, where the decision was made by this Authority not to take them into account because they were not authorized by or notified to this Authority at the time when this Authority began to draw up this report, and any accompanying letters (Rules 66.4bis, 70.2(e), 70.16 and 91.2). ☐ superseded sheets and any accompanying letters, where this Authority either considers that the superseding sheets contain an amendment that goes beyond the disclosure in the international application as filed, or the superseding sheets were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in item 4 of Box No. I and the Supplemental Box (see Rule 70.16(b)). b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing, in the form of an Annex C/ST.25 text file, as indicated in the Supplemental Box Relating to Sequence Listing (see paragraph 3ter of Annex C of the Administrative Instructions).			
4. This report contains indications relating to the following items: ☒ Box No. I Basis of the report ☐ Box No. II Priority ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☐ Box No. IV Lack of unity of invention ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement ☐ Box No. VI Certain documents cited ☒ Box No. VII Certain defects in the international application ☒ Box No. VIII Certain observations on the international application			
Date of submission of the demand 29.11.2019		Date of completion of this report 15.04.2020	
Name and mailing address of the international preliminary examining authority:  European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016		Authorized officer Kardinal, Siegmard Telephone No. +31 70 340-3483	



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2019/052069

Box No. I Basis of the report

1. With regard to the **language**, this report is based on
- ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a) and (b))
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-49 as originally filed

Claims, Numbers

1-21 filed in electronic form on

13-03-2020

- ☐ a sequence listing - see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since either they are considered to go beyond the disclosure as filed, or they were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in the Supplemental Box (Rules 70.2(c) and (c-bis)):
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
5. ☐ This report has been established:
- ☐ taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rules 66.1(d-bis) and 70.2(e)).
 - ☐ without taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91(Rules 66.4bis and 70.2(e)).

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2019/052069

6. ☒ With regard to top-up searches (Rules 66.1 *ter* and 70.2(f)):
- ☒ A top-up search was carried out by this Authority on 18.12.2019 (all discovered documents are listed in the Supplemental Box Relating to Top-up Search).
 - ☐ Additional relevant documents have been discovered during the top-up search.
 - ☐ No top-up search was carried out by this Authority because it would serve no useful purpose.
7. ☐ Supplementary international search report(s) from Authority(ies) has/have been received and taken into account in establishing this report (Rule 45bis.8(b) and (c)).

* If item 4 applies, some or all of those sheets may be marked "superseded".

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>2-5, 7-9, 11-13, 17-19, 21</u>
	No: Claims	<u>1, 6, 10, 14-16, 20</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-21</u>
Industrial applicability (IA)	Yes: Claims	<u>1-21</u>
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item I

- 1 The following amendments filed in electronic form on 13-03-2020 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT:
 - 1.1 Claim 1 has been amended to replace the original phrase "consisting essentially off" with the transitional phrase "comprising".

In the view of the Applicant, it is evident that this amendment does not add matter (see, for example, page 27, embodiment 1 of the original application for the use of "comprising").

However, it is noted that embodiment 1 on page 27 of the application as filed relates to subject-matter which is different from the method of original claim 1. It cannot provide a basis for the open-ended transitional term "comprising" in connection with the subject-matter of original claim 1. The original closed-ended transitional phrase "consisting essentially of" has a somewhat ambiguous yet limiting meaning (see [143] of the description) which is no longer present. The skilled reader is therefore confronted with new information.
 - 1.2 Claim 1 has been further amended to recite that the solvent mixture may have "a concentrated volume or a dry extract obtained from evaporation to dryness of the original volume of the solvent mixture". In the view of the Applicant, basis exists at paragraph 22 of the original application.

However, it is noted that paragraph [22] relates to a specific embodiment involving a decarboxylation. Such a decarboxylation is not a feature of step (a) of present claim 1. Paragraph [22] cannot provide a basis for introducing these amendments. Again, the skilled reader is confronted with new information.
- 2 The following amendments are based on the application as filed and do not introduce added subject-matter:
 - 2.1 The inclusion a step "(d) performing optional crystallization after the step of liquid:liquid chromatography" finds a generic basis at 28 of the original application.

However, it is noted that this feature is optional and has no limiting effect. Also no indirectly limiting effect for the presence additional crystallization steps.
 - 2.2 Claim 15 has been amended to delete wording already recited in claim 1.
 - 2.3 Claim 16 has been amended to refer to "plant material or extracts" and to "the plant material and the solvent mixture". Basis exists at paragraphs 22 and 65 of the original application.

The following opinion is based on the claims as filed on 13-03-2020 even though the amendments of claim 1 do not fulfil the requirements of Article 34(2)(b) PCT. This appears justified in the present case since the opinion on novelty and inventive step is not changed by the wording of claim 1 as "comprising" or "consisting essentially of". Also the scope of the closed-ended transitional phrase was construed broadly in view of the different embodiments of the claimed method disclosed in the application.

Re Item V

Reference is made to the following documents:

- D1 US 2018/000879 A1 (NADAL ROURA XAVIER) 4 January 2018
- D2 WO 2016/187679 A1 (POBELCH - GLE OOD) 1 December 2016
- D3 WO 2016/135346 A1 (BIONORICA ETHICS GMBH) 1 September 2016
(cited in the application)

3 Novelty (Article 33(2) PCT)

- 3.1 Irrespectively of whether claim 1 is worded as a "method consisting essentially of the following steps: (a) [...], (b) [...]; and (c) [...]." or a "method comprising" these steps (the present wording), the claim scope is construed broadly such that further steps like concentrating the liquid and purifying the product (e.g. (re)crystallizing it) before liquid-liquid chromatography (c) are deemed to be encompassed.

In this context it is noted that step (d) of "performing optional crystallization after the step of liquid:liquid chromatography" is optional and has no limiting effect, also no indirectly limiting effect for the presence of additional crystallization steps.

Furthermore, the process of present claim 1 can start from any plant material including plant extracts (see Item VIII, 1). That means additional steps can have taken place before arriving at the plant material of step (a).

- 3.2 D1 discloses (cf. examples 1, 10; paragraph [0062]) a method for purifying one or more cannabinoids from a plant material, including a step of countercurrent chromatography.

Example 1 of D1 is a method of isolating and purifying CBGA from *Cannabis sativa* L including incubating plant material with hexane and countercurrent chromatography using a two-phase system Hexane:Ethanol:Water (20:12:8).

The fact that the volume of hexane is reduced in the method of D1 from the original 750 ml to about 100 ml before the liquid-liquid chromatography and the solvent mixture is thereby purified by crystallization is covered by the scope of the present claim 1. It is not a differentiating feature. A crystallization step can be carried out before and/or after the liquid:liquid chromatography. The process of D1 uses "the raw or recrystallized CBGA", that is plant material obtained by crystallizing the extract or recrystallizing the plant material. This CBGA material includes the major cannabinoids present in the initial plant material.

In any, case, the process of present claim 1 can start from any plant material including plant extracts (see Item VIII, 1).

Example 10 of D1 discloses an analogous process which includes a step of decarboxylating the product such as to obtain CBG.

These processes of D1 fall within the scope of at least present claims 1, 6, 10, 14-16 and 20. The subject-matter of at least these claims is not novel.

4 Inventive step (Article 33(3) PCT)

4.1 Dependent claims 2-5, 7-9, 14-18, 22-25 and 27 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, the reasons being as follows:

Starting from document D1 as closest prior art, the features of these dependent claims may be considered to be the differentiating features. For none of these differentiating features a particular technical effect has been substantiated by means of suitable comparative examples. In each case, the objective technical problem can only be formulated as the provision of an alternative method for purifying one or more cannabinoids.

4.2 The use of countercurrent chromatography and centrifugal partitioning chromatography for the purification of cannabinoids is known to the skilled person from the prior art, e.g. D1 (cf. [0058] and the examples), D2 and D3 (cf. the passages indicated in the search report). Solvent systems including hexane, ethanol, acetonitrile, ethyl acetate, water and similar solvents are known (cf. D1, [0061]; D2, examples and D3, cf. the claims). It appears routine work for the person skilled in the art to choose suitable solvents for isolating THC-type extracts or CBD-type extracts. When doing so, the skilled person would consider using pentane (the lower homolog of hexane) in case of concerns about the toxicity of hexane and according to the circumstances. The skilled

person would thereby routinely arrive at solvent systems according to present claims 2 to 5, 19 and 21 in the expectation to provide an alternative purification method.

- 4.3 Concerning claims 7 to 9, Chemotypes I to IV of Cannabis sativa L and their main cannabinoids are known (see e.g. D1, [0045]). The skilled person would use them as starting materials depending on desired products.
- 4.4 Concerning dependent claims 11 and 17 the skilled person would routinely choose suitable known equipment and conditions according to the circumstances.
- 4.5 Concerning claims 12, 13 and 18, it is routine work of the skilled artisan to perform suitable further purification steps, including chromatographic purification (e.g. HPLC) or crystallisation in order to enhance the purity of the target compounds if desired and according to the circumstances.

Re Item VII

- 1 The description contains statements concerning the incorporation of priority or prior art documents by reference (see e.g. [1], [144]).
- 2 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1 is not mentioned in the description, nor is this document identified therein.
- 3 The list of "Aspects" expressed on pages 27 to 38 constitutes superfluous content and should be removed.

Re Item VIII

Clarity and support (Article 6 PCT)

- 1 Claim 1 starts from "a plant material". The nature of this plant material is not further defined. It may *include* a plant, a plant resin or a plant extract. But this list is not limiting. This holds even if the broad definition given in the description (see paragraph [56]) is taken into account. The term "plant extract" is rather vague and allows for the presence of an undefined number of preceding process steps for obtaining the plant extract. Hence, it is not clear how many preceding steps have taken place before arriving at the plant material of step (a). It could thus be argued that an extracted and recrystallised cannabinoid product is the "plant material" subjected to step (a) of claim 1.

- 2 The vague and imprecise statements in the description in paragraphs [136], [137], [139] implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.