PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	APR 19 2024
Applicant's or agent's file reference 54925-0003WO1	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 23/82367	04 December 2023 (04.12.2023)	05 December 2022 (05.12.2022)

International Patent Classification (IPC) or both national classification and IPC
IPC - INV. A61K 31/335, A61K 31/357, A61K 31/36 (2024.01)
ADD. A61K 31/33 (2024.01)
CPC - INV. A61K 31/335, A61K 31/357, A61K 31/36
ADD. A61K 31/33

Applicant MAPS PUBLIC BENEFIT CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ 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 Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and 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

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	25 March 2024 (25.03.2024)	Kari Rodriquez PCT Help Desk Telephone No. 571-272-4300

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ 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 (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(b)).

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed.

   b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.1(a)),

      ☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.

4. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established to the extent that a meaningful opinion could be formed without a WIPO Standard ST.26 compliant sequence listing.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 4-31

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 4-31 are so unclear that no meaningful opinion could be formed *(specify)*:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for said claims Nos. 4-31

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:

   ☐ paid additional fees.

   ☐ paid additional fees under protest and, where applicable, the protest fee.

   ☐ paid additional fees under protest but the applicable protest fee was not paid.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I: Claims 1-3 directed toward a composition comprising 3,4-methylenedioxymethamphetamine (MDMA), or a pharmaceutically acceptable salt and/or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the average particle size is from about 50 to about 400 micron.

Group II: Claim 32 directed toward a process for obtaining particles comprising crystalline 3,4- methylenedioxymethamphetamine (MDMA), or a pharmaceutically acceptable salt and/or solvate thereof, wherein the particles comprise particles that are substantially less than about 610 m; wherein the process comprises: (a) contacting a salt of MDMA with an organic solvent to obtain a first solution, (b) heating and stirring the first solution to obtain a second solution, (c) filtering the second solution to obtain a third solution, (d) cooling the third solution over a first time period to a first set temperature, (e) adding crystalline MDMA, or a pharmaceutically acceptable salt and/or solvate thereof seeds to the cooled solution of step (d) to obtain a fourth solution, (f) stirring the fourth solution of step (e) for a second time period at the first set temperature, (g) cooling the fourth solution of step (0 over a third time period to a second set temperature, (h) stirring the fourth solution of step (g) at the second set temperature for a fourth time period to obtain crystalline MDMA or a pharmaceutically acceptable salt and/or solvate thereof, (i) filtering the solution of step (h) to obtain particles of crystalline MDMA or a pharmaceutically acceptable salt and/or solvate thereof, (j) drying the particles of MDMA of step (i) at a set drying temperature under a set drying pressure for a set drying time period, and (k) milling the particles of step (j) under an inert atmosphere at a set milling speed and passing the milled particles through a mesh screen of a set size to obtain particles comprising crystalline 3,4-methylenedioxymethamphetamine (MDMA), or a pharmaceutically acceptable salt and/or solvate thereof.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features:

Group I requires a composition comprising 3,4-methylenedioxymethamphetamine wherein the average particle size is from about 50 to about 400 micron, not required by Group II

Group II requires a process for obtaining particles comprising crystalline 3,4- methylenedioxymethamphetamine wherein the process comprises: (a) contacting a salt of MDMA with an organic solvent, heating the solution, filtering the solution, cooling the solution, adding crystalline MDMA, or a pharmaceutically acceptable salt and/or solvate thereof seeds to the cooled solution, obtaining particles of crystalline MDMA, drying the particles of MDMA, and milling the particles, not required by Group I.

Common Technical Features:

Groups I-II share the common technical feature of a method of a composition comprising 3,4-methylenedioxymethamphetamine.

**********CONTINUED ON SUPPLEMENTAL PAGE**********

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-3

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-3	YES
	Claims	None	NO
Inventive step (IS)	Claims	None	YES
	Claims	1-3	NO
Industrial applicability (IA)	Claims	1-3	YES
	Claims	None	NO

2. Citations and explanations:

Claims 1-3 lack an inventive step under PCT Article 33(3) as being obvious over WO 2022/150525 A1 to Awakn Life Sciences (hereinafter "Awakn").

Regarding claim 1, Awakn discloses a composition (Para [02] Described herein are compositions of MDMA and methods of their use in MDMA- assisted psychotherapy) comprising 3,4-methylenedioxymethamphetamine (MDMA), or a pharmaceutically acceptable salt and/or solvate thereof (Para [27] the MDMA-assisted psychotherapy regimen comprises one or more non-drug psychotherapy sessions prior to and after administration of MDMA in conjunction with psychotherapy; Para [143] MDMA refers to 3,4-methylenedioxymethamphetamine) and one or more pharmaceutically acceptable excipients (Para [173] a composition containing such pure or substantially pure MDMA e.g., such MDMA plus an excipient, wherein excipient in some embodiments, refers to a substantially inactive substance that serves as the vehicle or medium) but does not disclose wherein the average particle size is from about 50 micron to about 400 micron. However, it would have been obvious to one of ordinary skill in the art to change the particle size through routine experimentation (Para [201] In preparing a formulation, it may be necessary to mill the active agent to provide the appropriate particle size prior to combining with the other ingredients).

Regarding claim 2, Awakn discloses the composition of claim 1, but does not disclose wherein the average particle size is from about 75 micron to about 200 micron. However, it would have been obvious to one of ordinary skill in the art to change the particle size through routine experimentation (Para [201] In preparing a formulation, it may be necessary to mill the active agent to provide the appropriate particle size prior to combining with the other ingredients).

Regarding claim 3, Awakn discloses the composition of claim 1 or 2, but does not disclose wherein the average particle size is from about 100 micron to about 200 micron. However, it would have been obvious to one of ordinary skill in the art to change the particle size through routine experimentation (Para [201] In preparing a formulation, it may be necessary to mill the active agent to provide the appropriate particle size prior to combining with the other ingredients).

Claims 1-3 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:
Box No. IV Lack of unity of invention

However, these shared technical features do not represent a contribution over prior art, because the shared technical feature is anticipated by WO 2022/150525 A1 to Awakn Life Sciences (hereinafter Awakn). Awakn discloses a composition (Para [02] Described herein are compositions of MDMA and methods of their use in MDMA- assisted psychotherapy) comprising 3,4-methylenedioxymethamphetamine (MDMA), or a pharmaceutically acceptable salt and/or solvate thereof (Para [27] the MDMA-assisted psychotherapy regimen comprises one or more non-drug psychotherapy sessions prior to and after administration of MDMA in conjunction with psychotherapy; Para [143] MDMA refers to 3,4-methylenedioxymethamphetamine).

As the shared technical features were known in the art at the time of the invention, they cannot be considered common technical features that would otherwise unify the groups. Therefore, Groups I-II lack unity under PCT Rule 13.

NOTE: Claims 4-31 are unsearchable claims because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).