IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Emergex USA Corporation
Serial No.: 17/997,094
Filing or 371(c) Date: 10/25/2022
Entitled: Transdermal Drug Delivery Devices Having Psilocybin, Lysergic Acid Diethylamide or 3,4-Methylenedioxymethamphetamine Coated Microprotrusions

Confirmation No.: 6919
Group No.:
Examiner:

THIRD-PARTY PRE-ISSUANCE SUBMISSION

Examiner:

The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application

1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021)
2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017)

Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list of the elements of the presently pending claims.

U.S.S.N. 17/997,094 Pending Claims	References
1. An intracutaneous delivery system comprising a plurality of microprojections that are adapted to penetrate or pierce the stratum corneum of a human patient, the microprojections having a coating thereon comprising a therapeutically effective amount of psilocybin, LSD or MDMA.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Claim 1** "A **transdermal** and/or topical pharmaceutical composition comprising: - about 0.1 % to about 20 % of an active agent selected from the group consisting of psilocybin, psilocin, **lysergic acid diethylamine (LSD),** and/or ibogaine, derivatives of these compounds, and combinations thereof…" From **Claim 7** "The pharmaceutical composition of any one of claims 1 to 6 which is formulated as a **transdermal patch**." From **Claim 12** "The pharmaceutical composition of any one of claims 1 to 11 which may be formulated as **microneedles**."
2. The system of claim 1, wherein at least 95% of the psilocybin, LSD or MDMA is released within about 20 minutes after application of the system to the stratum corneum of the human patient.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0019]** "…In this embodiment, the coating, upon its application to the skin via the microneedles, dissolves at a rate sufficient for rapid uptake of the drug into the epidermis and bloodstream. In one embodiment, **such rate is less than 20 minutes, or less than 15 minutes, or less than 10 minutes, or less than 5 minutes, or less than 2.5 minutes, or less than 1 minute**…"
3. The system of claim 2 wherein at least 95% of the psilocybin, LSD or MDMA is released within about 5 minutes after application of the system to the stratum corneum of the human patient.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0019]** "…In this embodiment, the coating, upon its application to the skin via the microneedles, dissolves at a rate sufficient for rapid uptake of the drug into the epidermis and bloodstream. In one embodiment, **such rate is less than 20 minutes, or less than 15 minutes, or less than 10 minutes, or less than 5 minutes, or less than 2.5 minutes, or less than 1 minute**…"
4. The system of claim 1, wherein the coating further comprises an excipient.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Page 41 lines 9-13** "As indicated the pharmaceutical formulations as disclosed herein may comprise auxiliary **excipients**

	such as for example diluents, binders, lubricants, surfactants, disintegrants, plasticisers, anti-tack agents, opacifying agents, pigments, and such like."
5. The system of claim 1, wherein the therapeutically effective amount of psilocybin, LSD or MDMA is about 1 mg to about 10 mg.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Page 15 lines 13-16** "In certain embodiments, **the dose of active agent is** greater than, for example, about 0.001, 0.00250.005, 0.0075, 0.01, 0.025, 0.05, 0.075, 0.1, 0.25, 0.75, **1, 2, 3, 4, 5, 6, 7, 8, 9, 10**, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 125, 150, 175, 200, 225, 250, or 275 **mg/day**." From **Claim 1** "A **transdermal** and/or topical pharmaceutical composition comprising: - about 0.1 % to about 20 % of an active agent selected from the group consisting of psilocybin, psilocin, **lysergic acid diethylamine (LSD),** and/or ibogaine, derivatives of these compounds, and combinations thereof…"
6. The system of claim 5, wherein the therapeutically effective amount of psilocybin, LSD or MDMA is about 2 mg to about 5 mg.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Page 15 lines 13-16** "In certain embodiments, **the dose of active agent is** greater than, for example, about 0.001, 0.00250.005, 0.0075, 0.01, 0.025, 0.05, 0.075, 0.1, 0.25, 0.75, 1, **2, 3, 4, 5,** 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 125, 150, 175, 200, 225, 250, or 275 **mg/day**. From **Claim 1** "A **transdermal** and/or topical pharmaceutical composition comprising: - about 0.1 % to about 20 % of an active agent selected from the group consisting of psilocybin, psilocin, **lysergic acid diethylamine (LSD),** and/or ibogaine, derivatives of these compounds, and combinations thereof…"
7. The system of claim 1, wherein the coating further comprises an acid.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **Claim 8** "The system of claim 1 wherein the solid formulation coating comprises about 20% to about 50% w/w zolmitriptan or salt thereof and **about 5% to about 20% w/w of an acid selected from the group consisting of malic acid, ascorbic acid, lactic acid, tartaric acid, citric acid, maleic acid, succinic acid and hydrochloric acid,** and wherein the composition is substantially free of a penetration enhancer."

8. The system of claim 7, wherein the acid is tartaric acid.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **Claim 8** "The system of claim 1 wherein the solid formulation coating comprises about 20% to about 50% w/w zolmitriptan or salt thereof and **about 5% to about 20% w/w of an acid selected from the group consisting of** malic acid, ascorbic acid, lactic acid, **tartaric acid,** citric acid, maleic acid, succinic acid and hydrochloric acid, and wherein the composition is substantially free of a penetration enhancer."
9. The system of claim 1, wherein the system is stable at room temperature for at least 6 months.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Page 54 lines 11-13** "Different techniques and ingredients **can be used to increase the stability** and/or solubility of the active ingredients in formulation such as without any limitation to coating, encapsulation, microencapsulation, nanoencapsulation, lyophilization, chelating agents, complexing agents, etc."
10. (canceled)	
11. A method for treating depression in a human patient in need thereof, comprising the steps of: (a) providing an intracutaneous delivery system comprising a plurality of microprojections that are adapted to penetrate or pierce the stratum corneum of a human patient, the microprojections having a coating thereon comprising a therapeutically effective amount of psilocybin, LSD or MDMA, (b) applying the microprojections to a selected area of skin of the patient.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Claim 1** "A transdermal and/or topical pharmaceutical composition comprising: - about 0.1 % to about 20 % of an active agent selected from the group consisting of psilocybin, psilocin, **lysergic acid diethylamine (LSD)**, and/or ibogaine, derivatives of these compounds, and combinations thereof…" From **Claim 7** "The pharmaceutical composition of any one of claims 1 to 6 which is formulated as a **transdermal patch**." From **Claim 10** "The pharmaceutical composition of any one of claims 1 to 9 indicated for the **treatment and/or prevention and/or control of severe depression (treatment resistant), major depressive disorder**, obsessive-compulsive disorder, post-traumatic stress disorder, quitting smoking, alcohol addiction, cocaine addiction, opioid addiction, anxiety (stress), adult ADHD, cluster headaches, and cancer related or other end-of-life psychological distress in a patient." From **Claim 12** "The pharmaceutical composition of any one of claims 1 to 11 which may be **formulated as microneedles**."

12. The method of claim 11, wherein at least 95% of the psilocybin, LSD or MDMA is released within about 20 minutes after application of the microprojections to the patient.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0019]** "…In this embodiment, the coating, upon its application to the skin via the microneedles, dissolves at a rate sufficient for rapid uptake of the drug into the epidermis and bloodstream. In one embodiment, **such rate is less than 20 minutes, or less than 15 minutes, or less than 10 minutes, or less than 5 minutes, or less than 2.5 minutes, or less than 1 minute**…"
13. (canceled)	
14. The method of claim 11, wherein the therapeutically effective amount of psilocybin, LSD or MDMA is about 1 mg to about 10 mg.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Page 15 lines 13-16** "In certain embodiments, **the dose of active agent is** greater than, for example, about 0.001, 0.00250.005, 0.0075, 0.01, 0.025, 0.05, 0.075, 0.1, 0.25, 0.75, **1, 2, 3, 4, 5, 6, 7, 8, 9, 10,** 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 125, 150, 175, 200, 225, 250, or 275 **mg/day**"
15. (canceled)	
16. The method of claim 11, wherein the system is self-administered.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Page 5 line 29-30 – page 6 line 1** "**Administration of a transdermal patch or transdermal composition does not require medical supervision as patients can topically apply the transdermal patch or transdermal composition themselves**"
17. The method of claim 11, wherein when the system is administered to a population of patients, a statistically significant number of patients are successfully treated for depression as measured by a method or scale selected from the group consisting of the Beck Depression Inventory (BDI), the Center for Epidemiologic Studies Depression Scale (CES-D), the EQ-5D, the HRSD, the MADRS, and combinations thereof.	1. Intl. Pat. App. Doc. No. WO2021209815 "Transdermal Micro-Dosing Delivery of Psychedelics Derivatives" (Published October 21, 2021) From **Claim 10** "The pharmaceutical composition of any one of claims 1 to 9 indicated for the treatment and/or prevention and/or control of **severe depression (treatment resistant), major depressive disorder**, obsessive-compulsive disorder, post-traumatic stress disorder, quitting smoking, alcohol addiction, cocaine addiction, opioid addiction, anxiety (stress), adult ADHD, cluster headaches, and cancer related or other end-of-life psychological distress in a patient."

18. The method of claim 12, wherein the wear time is about 5 to 30 minutes.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0095]** "…The **typical patch wear time is about 15 to 45 minutes or less**, decreasing the potential for skin irritation…"
19. The system of claim 1, wherein the coating is a solid coating.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0018]** "Preferably, the microprojection member includes a biocompatible coating formulation comprising the drug, such as zolmitriptan, in a dose sufficient to provide therapeutic effect. The coating may further comprise one or more excipients or carriers to facilitate the administration of the drug across the skin. For instance, the biocompatible coating formulation comprises zolmitriptan and a water-soluble carrier that is first applied to the microprojections in liquid form and then dried to form a **solid biocompatible coating**."
20. The system of claim 1, wherein the coating covers about 10% to 80% of the length of each microprojection measured from the tip to the base.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0099] to [0106]** "The present disclosure therefore encompasses microneedle arrays having the following features: Array size: About 1 to 6 cm^2 Density (microprojections/cm^2): At least about 10 microprojections/cm^2, or in the range of about 200 to 2000 microprojections/cm^2, or about 200 to 800 microprojections/cm^2, or about 300 to 500 microprojections/cm^2, or approximately 750 microprojections/cm^2 **Microprojection length**: About 25 to 400 microns, or about 300 to 400 microns, or about 75 to 300 microns, or about 100 to 250 microns, or about 200 to 225 microns, or about 210 microns. In other embodiments, the length is less than 1000 microns, or less than 700 microns, or less than 500 microns. Accordingly, the microneedles penetrate the skin at about 25 to 1000 microns. Tip/barb length: About 50 to 100 microns, or about 60 microns, or about 70 microns, or about 80 microns, or about 90 microns Microprojection width: About 10 to 500 microns, or about 100 to 400 microns, or about 100 to 200 microns, or about 200 to 400 microns, or about 250 to 400 microns, or about 300 microns, or about 100 microns, or about 120 microns, or about 130 microns, or about 140 microns, or about 150 microns

	Tip angle: about 30-70 degrees, or about 40-60 degrees or about 50 degrees or about 60 degrees Microprojection coatable amount: About 1 to 4 mg"
21. The system of claim 1, wherein the system comprises a disposable patch assembly having a plurality of microprojections disposed in an array of about 3 cm^2 to about 6 cm^2, the array having a density of about 200 to about 2000 microprojections/cm^2.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0099]** "The present disclosure therefore encompasses microneedle arrays having the following features: **Array size: About 1 to 6 cm^2** **Density (microprojections/cm^2): At least about 10 microprojections/cm^2, or in the range of about 200 to 2000 microprojections/cm^2**, or about 200 to 800 microprojections/cm^2, or about 300 to 500 microprojections/cm^2, or approximately 750 microprojections/cm^2"
22. The system of claim 1, wherein the microprojections are rectangular, with a triangular tip to facilitate penetration of the stratum corneum of a human.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0017]** "…**The microprojections are applied to the skin to deliver the drug** to the bloodstream or, more particularly, **are adapted to penetrate or pierce the stratum corneum** at a depth sufficient to provide a therapeutically effective amount to the bloodstream. In one embodiment, the insertion of the drug-coated microneedles into the skin is controlled by a hand-held applicator that imparts sufficient impact energy density in less than about 10 milliseconds."
23. The system of claim 1, wherein the microprojections have: (i) a length of about 25 to about 600 μm; (ii) a width of about 10 μm to about 500 μm; (iii) a thickness of about 1 μm to about 500 μm; and (iv) a tip angle of about 30 to about 70 degrees.	2. U.S. Pat. App. Pub. No. 2017/0239174 "Method of Rapidly Achieving Therapeutic Concentrations of Triptans for Treatment of Migraines" (Published August 24, 2017) From **[0099] to [0106]** "The present disclosure therefore encompasses microneedle arrays having the following features: Array size: About 1 to 6 cm^2 Density (microprojections/cm^2): At least about 10 microprojections/cm^2, or in the range of about 200 to 2000 microprojections/cm^2, or about 200 to 800 microprojections/cm^2, or about 300 to 500 microprojections/cm^2, or approximately 750 microprojections/cm^2

	Microprojection length: **About 25 to 400 microns, or about 300 to 400 microns, or about 75 to 300 microns, or about 100 to 250 microns, or about 200 to 225 microns, or about 210 microns. In other embodiments, the length is less than 1000 microns, or less than 700 microns, or less than 500 microns. Accordingly, the microneedles penetrate the skin at about 25 to 1000 microns.** Tip/barb length: About 50 to 100 microns, or about 60 microns, or about 70 microns, or about 80 microns, or about 90 microns **Microprojection width: About 10 to 500 microns, or about 100 to 400 microns, or about 100 to 200 microns, or about 200 to 400 microns, or about 250 to 400 microns, or about 300 microns, or about 100 microns, or about 120 microns, or about 130 microns, or about 140 microns, or about 150 microns** **Tip angle: about 30-70 degrees, or about 40-60 degrees or about 50 degrees or about 60 degrees** Microprojection coatable amount: About 1 to 4 mg**"**

Electronic Acknowledgement Receipt

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Warnings:					
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2	Third-Party Submission Under 37 CFR 1.290	Third-party-preissuance-submission.pdf	52798 2d388927333dc9e0e444802820715a924eb81ffe	no	2
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4	Evidence of Publication	1_WO2021209815A1.pdf	5310525 5e69a793f17e3622e5673721b66f269938196057	no	69
Warnings:					
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5	Evidence of Publication	2_US20170239174A1.pdf	6044450 097929f2c9e30495142a1168e22a357aef0d5056	no	53
Warnings:					
Information:					
6	Concise Description of Relevance	Claims_Chart.pdf	238786 8fa28780f8faae6bd821a4b874c109d5bad3761d	no	8
Warnings:					
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7	Fee Worksheet (SB06)	fee-info.pdf	37760 2878bc0f95b490b4980a5ab39234690ba0ec79bf	no	2

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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.