Patentability Assessment

What follows is a patentability assessment prepared by Porta Sophia for [____entity name____] regarding technology describing a combination of an empathogen and psychedelic agent to therapeutically treat neuropsychological disorders, enhance positive psychedelic effects, and reduce negative psychedelic effects. More specifically, the combination of MDMA and LSD is described along with prospective dosages of each.

For all individuals filing a U.S. patent application, there exists a duty to disclose to the USPTO all information which is relevant in assessing the patentability of the invention which is the subject of the patent application (37 CFR 1.56). Information herein therefore must be disclosed to the USPTO if this information is relevant to active or future patent application.

The following claim chart analyzes individual features (column 1) of the proposed technology along with prior art references (column 2) relevant to said feature's patentability. Descriptions of the prior art's relevance to core aspects of U.S. standards of patentability are also presented (column 3).

Following the claim chart there is a summary of the patentability of the proposed technology.

#	Feature	Prior art reference excerpt(s)	Remarks
1	Inducing the release of endogenous monoamines and stimulating 5-HT 2A receptors to enhance the positive therapeutic effects of a psychedelic.	LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **page 355** "The most prevalent observations were cannabis enhancing the effects of hallucinogens (n = 17) and MDMA (n = 7), **MDMA and hallucinogens enhancing each other** (n = 11), hallucinogens enhancing each other (n = 6), amphetamines (n = 8) and cocaine (n = 6) counteracting hallucinogens, and cocaine counteracting the effects of MDMA (n = 7)." SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8.	35 U.S.C. 103 Combined, the LICHT (2012), SESSA (2015) and WHITE (1996) references may be construed by an examiner to provide evidence that Feature 1 is obvious to someone skilled in the art because it has been previously demonstrated that drugs that induce the release of endogenous monoamines (MDMA) enhance the effects of psychedelics.

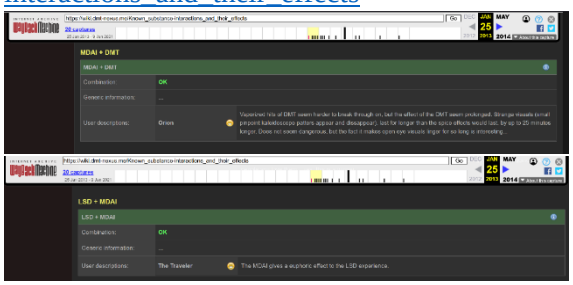
		From **page 3** "MDMA exerts its effects at **5-HT2A** and 5-HT2B receptors, creating feelings of reduced anxiety and depression and a sense of euphoria and well-being (Brunner and Hen, 1997; Graeff et al., 1996)." From **page 3** "Most psycholytic sessions began with **MDMA**, then **LSD** or 2-CB were added mid-way. Sometimes sessions began with **2-CB** or with LSD or on rare occasions other substances such as **ayahuasca** or **psilocybin** were used." WHITE (1996) "THE EFFECTS OF METHYLENEDIOXYMETHAMPHETAMINE (MDMA, "ECSTASY") ON MONOAMINERGIC NEUROTRANSMISSION IN THE CENTRAL NERVOUS SYSTEM" Progress in Neurobiology. 49, 455-479. From **page 456** "It is now well established that administration of single doses of **MDMA** to laboratory animals **induces acute increases in extracellular levels of the monoamines** serotonin (5HT), dopamine (DA) and norepinephrine (NE) in several brain regions"	
2	Administering a combination of an empathogen and a psychedelic to an individual.	LICHT (2012) "**Simultaneous polysubstance use** among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: **combination patterns** and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **page 355** "The most prevalent observations were cannabis enhancing the effects of hallucinogens (n = 17) and MDMA (n = 7), **MDMA and hallucinogens enhancing each other** (n = 11), hallucinogens enhancing each other (n = 6), amphetamines (n = 8) and cocaine (n = 6) counteracting hallucinogens, and cocaine counteracting the effects of MDMA (n = 7)."	35 U.S.C. 102 SCHECHTER (1998), LICHT (2012), SESSA (2015) each individually teach that the combination described in Feature 2 of an empathogen (MDMA) and hallucinogen/psychedelic (LSD) has been previously utilized and is in fact common. In our experience an examiner would

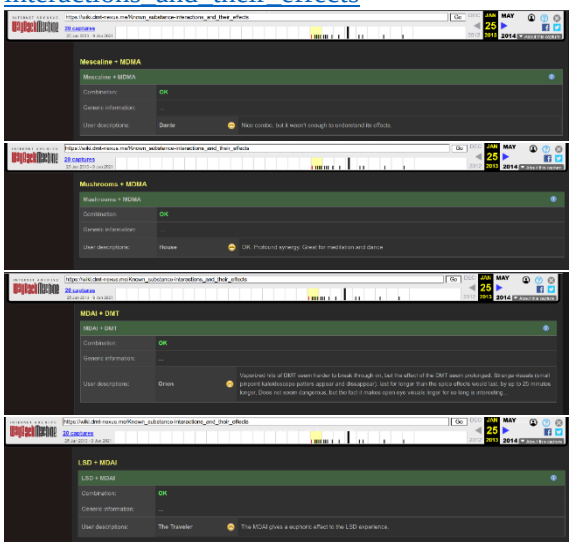
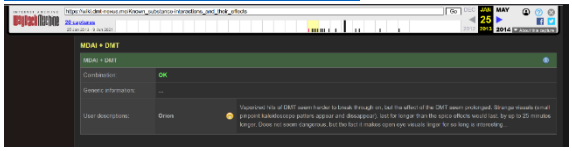
		SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions began with **MDMA, then LSD or 2-CB** were added mid-way. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used." SCHECHTER (1998) "`Candyflipping': Synergistic discriminative effect of LSD and MDMA" European Journal of Pharmacology. 341(2-3)131-134. From **page 132** "Interspersed between test/training maintenance with 1.5 mg/kg MDMA or saline sessions were test sessions in which the animal received either a low dose of **MDMA** (0.15 mg/kg) or a low dose of **LSD** (0.04 mg/kg) or **both drugs administered at the same time**."	likely consider this a violation of the novelty requirement.
3	Administering the empathogen/psychedelic combination in the same dosage form.	SCHECHTER (1998) "`Candyflipping': Synergistic discriminative effect of LSD and MDMA" European Journal of Pharmacology. 341(2-3)131-134. From **page 132** "Interspersed between test/training maintenance with 1.5 mg/kg MDMA or saline sessions were test sessions in which the animal received either a low dose of **MDMA** (0.15 mg/kg) or a low dose of **LSD** (0.04 mg/kg) or **both drugs administered at the same time**." From **page 132** "Both d,l-MDMA hydrochloride and d-LSD tartrate were received from the National Institute on Drug Abuse. **Solutions were made daily by dissolving in 0.9% saline vehicle and injected i.p. at a constant volume of 1 mg/kg**."	35 U.S.C. 103 SCHECHTER (1998) teaches that a combination of an empathogen and a psychedelic have previously been delivered at the same time and in similar formulations. Therefore, there exists the possibility that utilizing these drugs in the same dosage form would be considered obvious to

		Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a **pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 8** "The method of any one of the preceding claims, wherein **the pharmaceutical composition comprises a controlled release component and an immediate release component**." VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (**LSD**	someone skilled in the art. In addition, taken together, Int'l Pat. App. No. WO/2020/157569 , VAN WELL (2012), and HALBERSTADT (2018) suggest that multiple 5HT agonists, such as psychedelics and empathogens, can be utilized in a single pharmaceutical composition and therefore strengthen the likelihood that what is described in Feature 3 can possibly be construed as obvious to someone skilled in the art.

		binds to most 5-HT receptor sub-types as well as to dopaminergic and adrenergic receptors), it has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals."	
4	Administering the empathogen/psychedelic combination in a separate dosage forms.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA, then LSD or 2-CB were added mid-way.** Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used."	35 U.S.C. 102 SESSA (2015) describes administering a psychedelic and empathogen at separate times and therefore in separate dosage forms as described in Feature 4.
5	Administering the empathogen/psychedelic in the same dosage form with different release profiles.	Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a **pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 8** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component** and an **immediate release component**."	35 U.S.C. 103 Taken together, Int'l Pat. App. No. WO/2020/157569 , VAN WELL (2012), and HALBERSTADT (2018) suggest that multiple 5HT agonists, such as psychedelics and empathogens, can be utilized in a pharmaceutical composition with varying release components similar to what is described in Feature 5. Therefore, it may be construed as obvious to someone skilled in the art to have a first drug being delivered with

		VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (**LSD binds to most 5-HT receptor sub-types** as well as to dopaminergic and adrenergic receptors), it has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals."	one release profile and second drug being delivered with another.
6	The empathogen utilized in a psychedelic/empathogen combination is 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylendioxyamphetamine (MDA), 3,4,-methylenedioxyethylamphetamine (MDEA), 5,6-methylenedioxy-2-aminoindane (MDAI), mephedrone, methylone, 3-MMC, homologues thereof, analogues thereof, and prodrugs thereof.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used." CHARY (2018) "**Candyflipping and Other Combinations**: Identifying Drug–Drug Combinations from an Online Forum" Frontiers Psychiatry. 9:1-9.	35 U.S.C. 102 SESSA (2015), CHARY (2018), and DMT-NEXUS (2013) each individually teach that psychedelic combinations with empathogens included in Feature 6 such as MDMA, methylone, MDEA, and MDAI have been previously established.

		From **page 5** "In the synthetic hallucinogen, LSD is a hub that bridges two subislands. The left subisland of the hallucinogen island contains substances canonically thought to be anticholinergic. Hyoscine and hyoscyamine are tropane alkaloids found in jimson weed. The right subisland contains amphetamine derivatives, such as **MDMA** and the **MDMA derivatives** (bath salts), bk-MDMA (β-keto MDMA; **methylone**) and **bk-MDEA** (ethylone)." DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects 	
7	The emapthogen is MDMA at a dose of 20-200 mg.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "The choice and dosages of substances used for the sessions • **MDMA: 80–130 mg** • LSD: 50–200µg"	35 U.S.C. 102 SESSA (2015) teaches that the empathogen/psychedelic combination can include the empathogen MDMA in a dose within the range described in Feature 7.
8	The psychedelic is psilocybin, psilocin, lysergic acid diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI),	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8.	35 U.S.C. 102 SESSA (2015) and DMT-NEXUS (2013) each individually demonstrate empathogens have

	2,5-dimethoxy-4-bromoamphetamie (DOB), phenethylamine or tryptamine psychedelics, salts thereof, analogs thereof, prodrugs thereof, and homologues thereof.	From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as **ayahuasca** or **psilocybin** were used." DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects 	been combined with psychedelics listed in Feature 8 including LSD, DMT (ayahuasca), psilocybin/ psilocin (mushrooms) and mescaline.
9	The psychedelic is a short acting psychedelic. *Note: from discussions with the asking party (specifically email correspondence from October 2023) it was confirmed that DMT was referenced as a "short acting psychedelic"*	DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects 	35 U.S.C. 102 DMT-NEXUS (2013) demonstrates the utilization of DMT as the psychedelic portion of an empathogen/psychedelic combination as suggested in Feature 9.
10	The psychedelic is LSD at a dose of 0.05-0.3 mg.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes,	35 U.S.C. 102 SESSA (2015) teaches that the empathogen/psychedelic

		implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "The choice and dosages of substances used for the sessions • MDMA: 80–130 mg • **LSD: 50–200µg**"	combination can include the psychedelic LSD in a dose within the range described in Feature 10.
11	The empathogen is administered at a time before administering the psychedelic.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. Sometimes sessions **began with 2-CB or with LSD** or on rare occasions other substances such as **ayahuasca or psilocybin** were used."	35 U.S.C. 102 SESSA (2015) teaches that the empathogen/psychedelic combination can include the empathogen being administered first followed by the administration of a psychedelic, as described in Feature 11.
12	The empathogen is administered at the same time as administering the psychedelic.	SCHECHTER (1998) "`Candyflipping': Synergistic discriminative effect of LSD and MDMA" European Journal of Pharmacology. 341(2-3)131-134. From **page 132** "Interspersed between test/training maintenance with 1.5 mg/kg MDMA or saline sessions were test sessions in which the animal received either a low dose of **MDMA** (0.15 mg/kg) or a low dose of **LSD** (0.04 mg/kg) or **both drugs administered at the same time**."	35 U.S.C. 102 SCHECHTER (1998) teaches that both psychedelic and empathogenic drugs have previously been administered at the same time, as described in Feature 12.
13	The empathogen is administered after administering the psychedelic.	B-E-H, INC. (2012) "Searching for Samadhi in West Philadelphia LSD, MDMA (Ecstacy) & Alcohol" Erowid. Retrieved January 20, 2012. https://web.archive.org/web/20120120044616/https://erowid.org/experiences/exp.php?ID=79281 "Each person is to take 2 hits of **LSD** followed by 1 pill of **MDMA** approximately **3.5 hrs thereafter**."	35 U.S.C. 102 B-E-H, INC. (2012) teaches that it is known that one can administer a psychedelic prior to an empathogen, as described in Feature 13.

14	The empathogen is administered before and after administering the psychedelic.	KRYPTONITE (2009) "A Glorious New Year LSD & MDMA (Ecstasy)" Erowid. Retrieved July 4th, 2010. https://web.archive.org/web/20100704210848/https://www.erowid.org/experiences/exp.php?ID=58609 	35 U.S.C. 102 KRYPTONITE (2009) documents that the proposed dosing scheme described in Feature 14 of administering 1) an empathogen, 2) a psychedelic, 3) another dose of an empathogen is known.
15	The empathogen is administered 1-2 hours prior to the psychedelic.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used." KRYPTONITE (2009) "A Glorious New Year LSD & MDMA (Ecstasy)" Erowid. Retrieved July 4th, 2010. https://web.archive.org/web/20100704210848/https://www.erowid.org/experiences/exp.php?ID=58609 "I took a bottle of **liquid acid** to a friend's new year's eve party. I usually take **MDMA** with hallucinogens as it can help to reduce anxiety if things go pear-shaped. I was very fortunate in that I had managed to procure eight very clean* pills and took five of these at roughly two-hour intervals starting **two hours before the first dose of acid**."	35 U.S.C. 102 SESSA (2015) and KRYPTONITE (2009) each individually teach that MDMA can be administered prior to a psychedelic within the timeframe described in Feature 15.
16	The combination of an empathogen and a psychedelic is	Int'l Pat. App. Pub. No. WO/2021/202730 "MOLECULARLY-INITIATED, EXPERIENTIALLY-DELIVERED	35 U.S.C. 103 Int'l Pat. App. Pub. No.

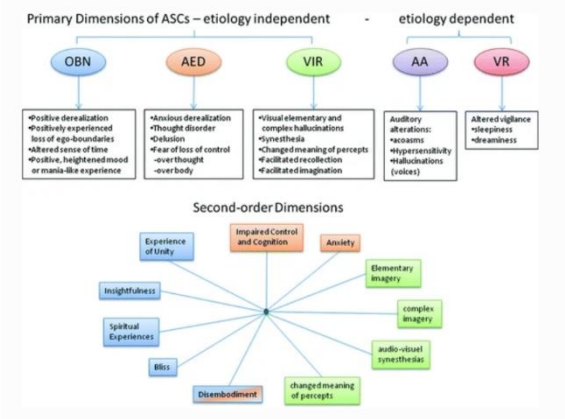
	administered to someone with a psychiatric disorder.	TREATMENTS AND SYSTEMS FOR PRACTICING SAME" (Published October 7, 2021) From **claim 3** "The method of claim 2, wherein the psychedelic agent is selected from the group consisting of: psilocybin, **3,4-Methylenedioxymethamphetamine (MDMA), lysergic acid diethylamide (LSD)**, N,N-Dimethyltryptamine (DMT), mescaline, peyote, 2,5-dimethoxy-4-bromophenethylamine (2C-B), 2,5-Dimethoxy-4-methylamphetamine (DOM), NBOMes (N-methoxybenzyl), **and any combination thereof**." From claim 14 "The method according to any one of claims 1 to 13, wherein the individual is suffering from a mental health condition selected from the group consisting of: **depression, anxiety**, post-traumatic stress disorder (PTSD), **addiction**, and any combination thereof." Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of **one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 43** "The method of any one of claims 1-38, wherein the neurological condition is **depression**, bipolar disorder, anxiety, social **anxiety**, post-traumatic stress disorder (PTSD), panic disorder, phobia, schizophrenia,	WO/2021/202730 teaches that a possible empathogen/psychedelic combination can be used to treat conditions that can be considered psychiatric in nature and therefore could lend credibility to the position that Feature 16 can be considered obvious to someone skilled in the art. This is further supported with the combined consideration of Int'l Pat. App. No. WO/2020/157569, VAN WELL (2012), and HALBERSTADT (2018).

		psychopathy, or **antisocial personality disorder**." From **claim 47** "The method of claim 46, wherein the compulsive disorder is **obsessive compulsive disorder (OCD)**, gambling, or aberrant sexual behavior." VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (LSD binds to most **5-HT** receptor sub-types as well as to dopaminergic and adrenergic receptors), it has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals"	
17	The combination is administered to someone with depression.	Int'l Pat. App. Pub. No. WO/2021/202730 "MOLECULARLY-INITIATED, EXPERIENTIALLY-DELIVERED TREATMENTS AND SYSTEMS FOR PRACTICING SAME" (Published October 7, 2021) From **claim 3** "The method of claim 2, wherein the psychedelic agent is selected from the group	35 U.S.C. 103 Int'l Pat. App. Pub. No. WO/2021/202730 suggests that drug combinations including the described empathogen/psychedelic

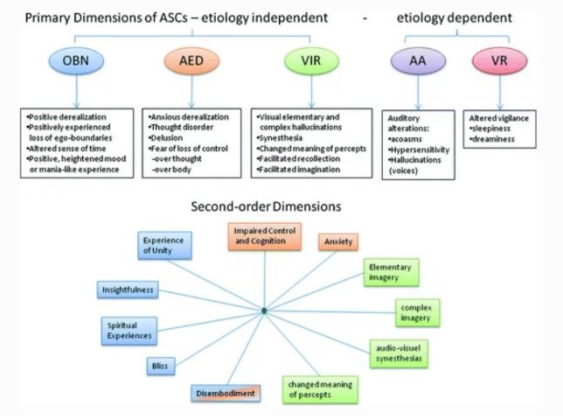
		consisting of: psilocybin, **3,4-Methylenedioxymethamphetamine (MDMA), lysergic acid diethylamide (LSD)**, N,N-Dimethyltryptamine (DMT), mescaline, peyote, 2,5-dimethoxy-4-bromophenethylamine (2C-B), 2,5-Dimethoxy-4-methylamphetamine (DOM), NBOMes (N-methoxybenzyl), **and any combination thereof**." From claim 14 "The method according to any one of claims 1 to 13, wherein the individual is suffering from a mental health condition selected from the group consisting of: **depression,** anxiety, post-traumatic stress disorder (PTSD), addiction, and any combination thereof."	combination can be used to treat many different disorders, including depression. This therefore lends credibility to the position that Feature 17 could be considered obvious to someone skilled in the art.
18	The combination is administered to someone with anxiety.	Int'l Pat. App. Pub. No. WO/2021/202730 "MOLECULARLY-INITIATED, EXPERIENTIALLY-DELIVERED TREATMENTS AND SYSTEMS FOR PRACTICING SAME" (Published October 7, 2021) From **claim 3** "The method of claim 2, wherein the psychedelic agent is selected from the group consisting of: psilocybin, **3,4-Methylenedioxymethamphetamine (MDMA), lysergic acid diethylamide (LSD)**, N,N-Dimethyltryptamine (DMT), mescaline, peyote, 2,5-dimethoxy-4-bromophenethylamine (2C-B), 2,5-Dimethoxy-4-methylamphetamine (DOM), NBOMes (N-methoxybenzyl), **and any combination thereof**." From claim 14 "The method according to any one of claims 1 to 13, wherein the individual is suffering from a mental health condition selected from the group consisting of: depression, **anxiety**, post-traumatic stress disorder (PTSD), addiction, and any combination thereof."	35 U.S.C. 103 Int'l Pat. App. Pub. No. WO/2021/202730 suggests that drug combinations including a possible empathogen/psychedelic combination can be used to treat several disorders including anxiety and therefore lends credibility to the position that Feature 18 would be considered obvious to someone skilled in the art.
19	The combination is administered to someone with obsessive-compulsive disorder.	Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF	35 U.S.C. 103 Int'l Pat. App. No. WO/2020/157569

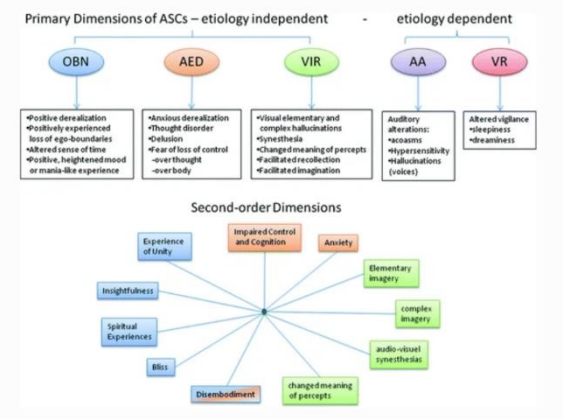
		PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of **one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From claim 46 "The method of any one of claims 1-38, wherein the neurological condition is a compulsive disorder." From **claim 47** "The method of claim 46, wherein the compulsive disorder is **obsessive compulsive disorder (OCD)**, gambling, or aberrant sexual behavior." VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (LSD binds to most **5-HT** receptor sub-types as well as to dopaminergic and adrenergic receptors), it	combined with VAN WELL (2012) and HALBERSTADT (2018) teaches that there exists the potential to use an empathogen/psychedelic combination to treat obsessive compulsive disorder and therefore lends credibility to the position that Feature 19 could be considered obvious to someone skilled in the art.

		has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals"	
20	The combination is administered to someone with substance abuse.	Int'l Pat. App. Pub. No. WO/2021/202730 "MOLECULARLY-INITIATED, EXPERIENTIALLY-DELIVERED TREATMENTS AND SYSTEMS FOR PRACTICING SAME" (Published October 7, 2021) From **claim 3** "The method of claim 2, wherein the psychedelic agent is selected from the group consisting of: psilocybin, **3,4-Methylenedioxymethamphetamine (MDMA), lysergic acid diethylamide (LSD)**, N,N-Dimethyltryptamine (DMT), mescaline, peyote, 2,5-dimethoxy-4-bromophenethylamine (2C-B), 2,5-Dimethoxy-4-methylamphetamine (DOM), NBOMes (N-methoxybenzyl), **and any combination thereof**." From claim 14 "The method according to any one of claims 1 to 13, wherein the individual is suffering from a mental health condition selected from the group consisting of: depression, anxiety, post-traumatic stress disorder (PTSD), **addiction**, and any combination thereof."	35 U.S.C. 103 Int'l Pat. App. Pub. No. WO/2021/202730 suggests that the empathogen/psychedelic combination can be used to treat substance abuse (addiction) and therefore lends credibility to the position that Feature 20 is obvious to someone skilled in the art.
21	The combination is administered to reduce bad drug effects.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. **Sometimes sessions** began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or **psilocybin were used**." From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the	35 U.S.C. 103 SMIGIELSKI (2019) and HALBERSTADT (2018) teaches that there is potential for bad drug effects to occur when psychedelics are used, however, no such bad effects/adverse reactions were seen in the combined drug

		qualitative outcomes were overwhelmingly positive. There were **no serious adverse reactions** to the substances, **no psychoses**, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe improvements in their relationships and well-being at home and work." SMIGIELSKI (2019) "Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat" Scientific Reports. 9:1-13. From **page 2** "Although the content and intensity of psychedelic experiences depend most critically on dosage, the same dose can induce a pleasurable state of self-dissolution or, under certain circumstances, a more distressing response associated with **thought disturbances, fear of losing control, anxiety, or panic**." From **page 3** "5D-ASC is designed to quantify positive and **negative forms of self/ego-dissolution**, including perceptual alterations." HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 227**  	sessions described in SESSA (2015). Therefore, it could be interpreted to suggest that the empathogen/psychedelic drug combination may play a part in mitigating bad drug effects associated with psychedelics, making Feature 21 potentially obvious to someone skilled in the art.

22	The combination administered reduces the bad drug effect of fear.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were **no serious adverse reactions** to the substances, **no psychoses**, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe improvements in their relationships and well-being at home and work." SMIGIELSKI (2019) "Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat" Scientific Reports. 9:1-13. From **page 2** "Although the content and intensity of psychedelic experiences depend most critically on dosage, the same dose can induce a pleasurable state of self-dissolution or, under certain circumstances, a more **distressing response associated with** thought disturbances, **fear of losing control**, anxiety, or panic." HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 227**	35 U.S.C. 103 SMIGIELSKI (2019) and HALBERSTADT (2018) teach that there is potential for fear to occur when psychedelics are used, however, no such bad effects/adverse reactions were seen in the combined drug sessions described in SESSA (2015). Therefore, it could be interpreted to suggest that the empathogen/psychedelic drug combination may play a part in mitigating bad drug effect of fear associated with psychedelics, making Feature 22 potentially obvious to someone skilled in the art.

			
23	The combination administered reduces the bad drug effect of paranoia.	SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were **no serious adverse reactions** to the substances, **no psychoses**, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe improvements in their relationships and well-being at home and work." SMIGIELSKI (2019) "Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat" Scientific Reports. 9:1-13. From **page 2** "Although the content and intensity of psychedelic experiences depend most critically on dosage, the same dose can induce a pleasurable state of self-dissolution or, under certain circumstances, a more distressing response associated with **thought disturbances**, fear of losing control, anxiety, or panic."	<u>35 U.S.C. 103</u> SMIGIELSKI (2019) and HALBERSTADT (2018) teach that there is potential for bad drug effects similar to paranoia (such as "thought disturbances") to occur when psychedelics are used, however, no such bad effects/adverse reactions were seen in the combined drug sessions described in SESSA (2015). Therefore, it could be interpreted to suggest that the empathogen/psychedelic drug combination may play a part in mitigating bad drug effects similar to paranoia associated with psychedelics, making Feature 23 potentially

		HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 227** 	obvious to someone skilled in the art.
24	The combination administered improves good drug effects.	LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **page 355** "The most prevalent observations were cannabis enhancing the effects of hallucinogens (n = 17) and MDMA (n = 7), **MDMA and hallucinogens enhancing each other (n = 11)**, hallucinogens enhancing each other (n = 6), amphetamines (n = 8) and cocaine (n = 6) counteracting hallucinogens, and cocaine counteracting the effects of MDMA (n = 7). SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 4** "**Spiritual insights** provide an awareness of being part of a greater whole, something bigger than oneself. Clients often state that underlying all experience is the concept of love; **binding together all other**	35 U.S.C. 103 LICHT (2012) teaches that MDMA and hallucinogens (a class of drugs that includes psychedelics) enhance one another, and SESSA (2015) teaches that, in response to the psychedelic/empathogen drug combination, individuals responded very positively to treatment. Therefore, it may be considered obvious that one would have expected to see the positive response/good drug effects, and that these effects may be possibly enhanced as described in

		aspects of life. This is very powerful for clients who have up till now never enjoyed any significant experience of love. **Feeling love** is a fundamental characteristic of psychedelic substances and particularly MDMA. The substance gives the clients an opportunity to see themselves as loving and, crucially, lovable individuals, which offers immense healing potential for clients with traumatic histories." From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were no serious adverse reactions to the substances, no psychoses, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe **improvements in their relationships** and **well-being** at home and work."	Feature 24 resulting from treatments similar to those described in SESSA (2015).
25	The combination administered improves the good drug effect of love.	LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **page 355** "The most prevalent observations were cannabis enhancing the effects of hallucinogens (n = 17) and MDMA (n = 7), **MDMA and hallucinogens enhancing each other (n = 11)**, hallucinogens enhancing each other (n = 6), amphetamines (n = 8) and cocaine (n = 6) counteracting hallucinogens, and cocaine counteracting the effects of MDMA (n = 7). SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 4** "Spiritual insights provide an awareness of being part of a greater whole,	35 U.S.C. 103 LICHT (2012) teaches that MDMA and hallucinogens (a class of drugs that includes psychedelics) enhance one another, and SESSA (2015) teaches that feeling love is a common response to psychedelic or empathogen use. Therefore, it may be considered obvious that one would have expected to see Feature 25's enhanced love response resulting from the combination treatment

		something bigger than oneself. Clients often state that underlying all experience is the concept of love; binding together all other aspects of life. This is very powerful for clients who have up till now never enjoyed any significant experience of love. **Feeling love is a fundamental characteristic of psychedelic substances and particularly MDMA**. The substance gives the clients an opportunity to see themselves as loving and, crucially, lovable individuals, which offers immense healing potential for clients with traumatic histories." From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were no serious adverse reactions to the substances, no psychoses, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe **improvements in their relationships** and **well-being** at home and work."	described in SESSA (2015).
26	The combination administered improves the good drug effect of experience of unity.	LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **page 355** "The most prevalent observations were cannabis enhancing the effects of hallucinogens (n = 17) and MDMA (n = 7), **MDMA and hallucinogens enhancing each other (n = 11)**, hallucinogens enhancing each other (n = 6), amphetamines (n = 8) and cocaine (n = 6) counteracting hallucinogens, and cocaine counteracting the effects of MDMA (n = 7). SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8.	35 U.S.C. 103 LICHT (2012) teaches that MDMA and hallucinogens (a class of drugs that includes psychedelics) enhance one another, and SESSA (2015) teaches that feelings that can be considered similar to unity (described as a "binding together all other aspects of life") is a common response to psychedelic and empathogen use. Therefore, it may be considered

		From **page 4** "**Spiritual insights** provide an awareness of being part of a greater whole, something bigger than oneself. Clients often state that underlying all experience is the concept of love; **binding together all other aspects of life**. This is very powerful for clients who have up till now never enjoyed any significant experience of love. Feeling love is a fundamental characteristic of psychedelic substances and particularly MDMA. The substance gives the clients an opportunity to see themselves as loving and, crucially, lovable individuals, which offers immense healing potential for clients with traumatic histories." From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were no serious adverse reactions to the substances, no psychoses, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe **improvements in their relationships** and well-being at home and work."	obvious that one would have expected to see an enhanced feeling such as that described in Feature 26 in response to administering the combination treatment.
27	The combination administered improves the good drug effect of insightfulness.	LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **page 355** "The most prevalent observations were cannabis enhancing the effects of hallucinogens (n = 17) and MDMA (n = 7), **MDMA and hallucinogens enhancing each other (n = 11)**, hallucinogens enhancing each other (n = 6), amphetamines (n = 8) and cocaine (n = 6) counteracting hallucinogens, and cocaine counteracting the effects of MDMA (n = 7). SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group	35 U.S.C. 103 LICHT (2012) teaches that MDMA and hallucinogens (a class of drugs that includes psychedelics) enhance one another, and SESSA (2015) teaches that insightfulness is a common response to psychedelic and empathogen use. Therefore, it may be considered obvious that one would have expected to see an

		psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 4** "**Spiritual insights provide an awareness of being part of a greater whole, something bigger than oneself**. Clients often state that underlying all experience is the concept of love; binding together all other aspects of life. This is very powerful for clients who have up till now never enjoyed any significant experience of love. Feeling love is a fundamental characteristic of psychedelic substances and particularly MDMA. The substance gives the clients an opportunity to see themselves as loving and, crucially, lovable individuals, which offers immense healing potential for clients with traumatic histories." From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were no serious adverse reactions to the substances, no psychoses, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe improvements in their relationships and well-being at home and work."	enhanced insightful feeling described in Feature 27 resulting from the combination treatment described in SESSA (2015).
28	The administration of the combination wherein the empathogen reduces anxiety up to 6 hours after said administration.	LIECHTI (2001) "Gender differences in the subjective effects of MDMA" Psychopharmacology. 154, 161–168. From **page 163** "F and P values for significant main effects and interactions are presented in Table 1. **Subjective effects of MDMA began 30–60 min after MDMA administration, peaked at 75–120 min, and lasted for a mean duration of 3.5h**." SANTOS-LONGHURST (2020) "LSD and MDMA: What to Know About Candyflipping" Healthline. Retrieved February 11 2020. https://web.archive.org/web/20200211232126/h	35 U.S.C. 103 LIECHTI (2001) teaches that the effects of MDMA can last several hours, up to 6 hours as described by SANTOS-LONGHURST (2020). DANFORTH (2016) additionally teaches that MDMA-assisted therapy can reduce anxiety. Therefore, it may

		ttps://www.healthline.com/health/lsd-and-mdma "**MDMA**, which is usually taken several hours after LSD, typically kicks in within 20 to 70 minutes and lasts from **3 to 6 hours**." DANFORTH (2016) "MDMA-assisted therapy: A new treatment model for social anxiety in autistic adults" Progress in Neuro-Psychopharmacology and Biological Psychiatry. 64:237-249. From **page 237** "**MDMA-assisted therapy could reduce social anxiety** symptoms and increase social adaptability."	be considered obvious that a combination therapy using an empathogen would likewise result in Feature 28's anxiety relief response over a similar period of time.

Assessment Summary

Subject Matter Eligibility (35 U.S.C. 101)

> *35 U.S.C. 101 permits a patent to be granted only for any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof. The disclosed invention must be a process, machine, manufacture, or composition of matter and cannot be an abstract idea, law of nature, or natural phenomenon (including a product of nature).*

The currently disclosed invention, described above in Features 1 though 28, is a combination of a psychedelic and an empathogenic pharmaceutical which can be in single or multiple dosage units of various release profiles. This is a composition of matter that is not an abstract idea, law of nature, or natural phenomenon and therefore it is unlikely from our experience that an examiner would state that this disclosed invention would violate 35 U.S.C. 101.

Novelty (35 U.S.C. 102)

> *35 U.S.C. 102 describes that a person shall be entitled to a patent unless 1) claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention or 2) the claimed invention was described in a patent issued or in an application for patent published/deemed published which names another inventor and was effectively filed before the effective filing date of the claimed invention.*

Due to the existence of prior art demonstrating lack of novelty of many disclosed features, from our experience there is a high probability of an examiner challenging the novelty of the disclosed invention at multiple points – specifically Features 2, 4, and 6-15. These features of the proposed invention have been well documented in various forms of prior art, including peer reviewed journal references (SCHECHTER (1998), LICHT (2012), SESSA (2015), and CHARY (2018)) as well as public online forum entries (KRYPTONITE (2009), B-E-H, INC. (2012), and DMT-NEXUS (2013)). Together these references can likely be utilized as strong evidence of anticipation of potential claims relating to the proposed combination (Feature 2) in separate dosage forms (Feature 4) using many of the same empathogens (Feature 6) and psychedelics (Feature 8 and Feature 9) within the same dosage ranges (Feature 7 and Feature 10) in the same dosing schemes (Features 11 through 15). From our experience, this information, as presented in these features, would likely receive a rejection because it doesn't meet the standards of novelty described in 35 U.S.C. 102.

Nonobviousness (35 U.S.C. 103)

> *35 U.S.C.103 sets forth the nonobviousness requirement for patentability. The claimed invention as a whole should not have been obvious to someone skilled in the art of the claimed invention before the effective filing date of the claimed invention.*

Because of the existence of a substantial set of relevant prior art describing similar technology (when considered alone or with other pieces of prior art), from our experience there is a high probability of an

examiner challenging that Features 1, 3, 5, and 16-28 of the disclosed invention would be considered obvious to someone skilled in the art. These features of the proposed invention have been documented or suggested in various forms of prior art including peer reviewed journal references (WHITE (1996), SCHECHTER (1998), LIECHTI (2001), LICHT (2012), VAN WELL (2012), SESSA (2015), HALBERSTADT (2018), SMIGIELSKI (2019), and SANTOS-LONGHURST (2020)) as well as patent documents (Int'l Pat. App. Pub. No. WO/2020/157569 and Int'l Pat. App. Pub. No. WO/2021/202730). There is a strong likelihood that these references, taken together, can be utilized in establishing the obviousness of potential claims derived from features such as simulating an enhanced positive response to a psychedelic through stimulating endogenous monoamines release via 5-HT2A receptor activation (Feature 1), utilizing a psychedelic combined with an empathogen in the same dosage form (Feature 3), possibly with different release profiles (Feature 5) to treat psychiatric disorders (Feature 16) like depression (Feature 17), anxiety (Feature 18), obsessive compulsive disorder (Feature 19) and addiction (Feature 20), and reduce bad drug effects (Features 21-23) while improving good drug effects (Features 24-27) while the empathogen has the effect of reducing anxiety in an individual up for a period of time after the combination is administered (Feature 28). From our experience, this information, as presented in these features, typically receive a rejection by the examiner for failing to meet the standards of nonobviousness described in 35 U.S.C. 103.

Enablement & Written Description (35 U.S.C. 112)

> *35 U.S.C. 112 requires that a full and clear description of the invention for which a patent is sought and the patentee must disclose sufficient information to demonstrate that the inventor had possession of the invention at the time of filing and to enable those skilled in the art to make and use the invention. Applicants cannot conceal from the public the best way of practicing the invention that was known to the patentee at the time of filing the patent application and failure to fully comply with the disclosure requirements could result in the denial of a patent, or in a holding of invalidity of an issued patent.*

It is essential that the applicant provide a complete and clear description of the invention for which they are submitting a patent application to meet the standard of enablement. Given that no draft of the specification for the proposed invention was provided, an assessment regarding potential enablement issues cannot effectively be made.

Overall, all features of the proposed invention are likely to face challenges by the USPTO on the grounds of novelty or obviousness. The feature least established in prior art is Feature 3, relating to the proposed drug combination being utilized in the same dosage form. However, there is currently a lack of experimental data that can be used to assist in establishing potential claims based off this feature. It is suggested that the asking party run further experiments demonstrating the therapeutic viability of the single dosage form of the proposed psychedelic/empathogen combination to better establish potential patentability of the proposed formulation(s) and uses thereof.