UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Gilgamesh Pharmaceuticals, Inc.,

Petitioner

v.

Enveric Biosciences Canada, Inc.

Patent Owner

Case _____

Patent No. 12,138,276

PETITION FOR POST GRANT REVIEW

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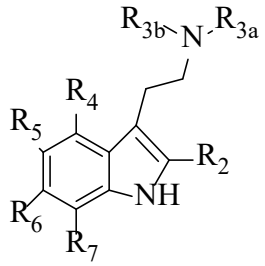
TABLE OF EXHIBITS

Exhibit No.	Description
1001	U.S. Patent No. 12,138,276 to Hagel, et al., issued November 12, 2024 (" '276 patent")
1002	Certificate of Correction issued April 22, 2025 for the '276 patent
1003	Jalal Soubhye, et al., *Structure-Based Design, Synthesis, and Pharmacological Evaluation of 3-(Aminoalkyl)-5-fluoroindoles as Myeloperoxidase Inhibitors*, J. MED. CHEM. 2010, 53, 8747-8759
1004	Asher Kalir, et al., *Synthesis and Pharmacological Activity of Alkylated Tryptamines*, ALKYLATED TRYPTAMINES 1966, 9, 341-344
1005	Z. Pelchowicz, et al., *N-Alkylated 5-Fluorotryptamines*, JOURNAL OF ISRAEL INSTITUTE FOR BIOLOGICAL RESEARCH 1961, 5418-5421, available at http://pubs.rsc.org | doi:10.1039/JR9610005418
1006	European Patent Application Publication No. EP 2682119 A1 to Jalal Soubhye, et al., published 08/01/2014
1007	U.S. Patent No. 3,780,063 to George Edward Van Lear, et al., issued December 18, 1973 ("US '063")
1008	U.S. Patent Publication No. 2012/0122948 A1 to Jalal Soubhye, et al., published May 17, 2012 ("US '048")
1009	U.S. Provisional Application No. 62/978,075 to Andrew Carry Kruegel, et al., filed February 18, 2020 ("USSN '075)
1010	U.S. Patent No. 11,440,879 to Andrew Carry Kruegel, issued September 13, 2022 ("US '879")

1011	U.S. Patent Publication No. 2012/0029010 A1 to Mark T. Hamann, et al., published February 2, 2012 ("US '010")
1012	International Patent Publication No. WO 2018/106907 A1 to Kenneth Batchelor, et al., published June 14, 2018 ("WO '907")
1013	Adrian Hall, et al., *Discovery of a novel indole series of EP1 receptor antagonists by scaffold hopping*, BIOOGANIC & MEDICINAL CHEMISTRY LETTERS 2008, 18, 2684-2690
1014	International Patent Publication No. WO 2020/181194 A1 to Paolo L. Manfredi, et al., published September 10, 2020 ("WO '194")
1015	Marc Julia, et al., *Synthesis of aminoindoles in position 4 or 5 through "arynic" substitution*, C. R. ACAD. SC. PARIS 1967, 265, 110-112 Accompanied By Certified Translation
1016	Walter Jantschko, et al., *Exploitation of the unusual thermodynamic properties of human myeloperoxidase in inhibitor design*, BIOCHEMICAL PHARMACOLOGY 2005, 69, 1149-1157

I. PRELIMINARY STATEMENT

Claimed subject matter of U.S. Patent No.12,138,276 ("the '276 patent") is either not novel or is an obvious combination of known elements for use in the treatment of psychiatric disorders in a subject. The '276 patent lacks enabling support. The '276 patent claims, *inter alia*, a chemical compound or salt thereof having the formula (I)



(I)

wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.

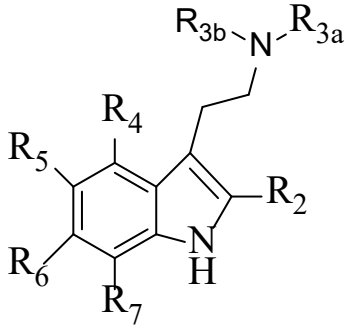
Most of the claimed subject matter is anticipated by prior art, which the Examiner during prosecution never found. Claims 1-20 and 24, 26-28 are invalid as being anticipated under 35 U.S.C. §102(a)(1) and/or 102(b)(1) by prior art. Further, claims 25 and 29 are invalid under 35 U.S.C. §103 as defining subject as being obvious from combination of elements of the prior art. Claim 1 is indefinite and not enabled.

Petitioner respectfully submits that this Post Grant Review (PGR) should be instituted and that claims 1- 20 and 24-29 be held unpatentable.

II. THE '276 PATENT (EX 1001)

A. '276 Specification

The '276 Patent (EX 1001) describes "halogenated psilocybin derivatives and compounds and pharmaceutical and recreational drug formulations containing the same." EX 1001 at Abstract. In an embodiment, it provides a chemical compound of Formula I or a salt of Formula I



I

wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group. EX 1001 at column 2, lines 20-39. It discloses various embodiments therein. EX 1001, at column 2, line 40 to column 6, line 66. The compound of Formula I is prepared "using a biosynthetic system which comprises cells comprising a psilocybin enzyme complement." EX 1001 at Abstract. The compounds of formula I are produced by contacting a halogenated psilocybin precursor compound with a host cell comprising a psilocybin biosynthetic enzyme complement; and growing the host cell to produce a halogenated psilocybin compound or salt thereof having Formula I. EX 1001, at column 53, lines 15-47. The specification exemplifies several halogenated psilocybin precursor compounds, for example, halogenated tryptophan halogenated tryptamine, halogenated 4-hydroxyindole, halogenated 4-hydroxytryptophan, halogenated 4-hydroxytryptamine; halogenated norbaeocystin and halogenated baeocystin, especially 2-5-6, and 7-halogenated forms of the foregoing. EX 1001, column 53, line 59- column 54, line 3. According to the '276 patent, the host cell includes a psilocybin biosynthetic enzyme, which is either naturally present or, if not naturally present, the host cell can be modulated to produce a psilocybin biosynthetic enzyme complement by introducing a nucleic acid sequence encoding a psilocybin biosynthetic enzyme complement into the host cell, which can make the psilocybin biosynthetic enzyme complement upon cell growth. EX 1001, column 54, lines 9-32. Various nucleic acid sequences encoding one or more enzymes constituting a psilocybin biosynthetic

enzyme complement are provided. See, EX 1001, column 54, line 56 to column 55, line 31. The specification lists various host cells, such as, for example, microbial cells, e.g., bacterial cells, yeast cells, algal cells, or plant cells. EX 1001, column 54, lines 33-38. According to the specification, techniques for introducing nucleic acid material into the host are known in the art. EX 1001, column 54, lines 33- 55. Illustrations describing the general technique of the molecular cloning method for introducing nucleic acid sequences encoding one or more enzymes constituting a psilocybin biosynthetic enzyme complement, growing the host cells, introducing halogenated psilocybin precursor compounds into the host cells and separating the halogenated psilocybin compounds from the host cell is described in EX 1001, column 55, line 37 to column 63, line 14. The compound of Formula I is alleged to be useful as a recreational drug and as a drug useful for treating psychiatric disorders. EX 1001, at column 7, lines 1-64; column 51, line 10 to column 52, line 10.

B. Prosecution History (EX 1002)

The underlying application of the '276 Patent was filed in the United States Patent and Trademark Office ("USPTO") on May 6, 2024, and was assigned USSN 18/655,793. It is a continuation of USSN 17/903,080 filed on Sept. 6, 2022, now US Patent No. 11,998,557, which is a continuation of international application having serial number PCT/CA2021/051209, filed on September 1. 2021, and claiming priority of provisional application USSN 63/073,104, filed on September 1, 2020. The inventors listed on the '276 patent are Jillian A. Hagel and Peter J. Facchini, and the applicant is listed as Enveric Biosciences Canada, Inc.

The original application, as filed, contained 30 claims, of which only claim 1 was independent.

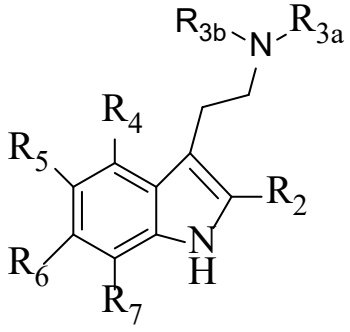
The prosecution history was simple, with no substantive rejections of prior art by the USPTO. The applicant requested prioritized examination under 37 C.F.R. §1.102(e), which was granted. A Restriction Requirement issued, under 35 U.S.C. §121, alleging that claims 1-29, directed to compounds or pharmaceutical compositions and claim 30, directed to a method of use, defined two separate inventions. The USPTO requested that applicant elect one group for examination and elect a species. Applicant elected claims 1-29 for continued examination without traverse, electing the species depicted as compound V, using the variables of Formula I,

R_2, R_6 and R_7 are H, R_4, and R_5 are F, R_{3a} is –(C=O)CH_3(C=O)(C_1-C_6) alkyl and R_{3b} is H. In addition, applicant amended claim 1 by capitalizing the first word therein. Applicant held a telephonic interview with the Examiner who proposed to the applicant that it file terminal disclaimers over the parent patents to overcome an obviousness-types double patenting rejection, which was presented as being the only rejection to be raised by the USPTO. Applicant filed two terminal disclaimers with respect to US Patent Nos. 11,998,557 and 11,918,594. The terminal disclaimers were approved by the USPTO. A Notice of Allowance was mailed. In the Notice of Allowance, the Examiner cancelled claim 30. The issue fee was paid, and the '276 patent issued on Nov. 12, 2024. Subsequently, applicant filed two Certificates of Correction in which the applicant corrected an obvious typographical error in the formula of compound XXIII in claim 27, wherein the amine nitrogen was not drawn. The first request for the Certificate of Correction was denied, the second request was granted.

C. Claims of the '276 Patent That Are Invalid

Following the entry of the Certificate of Correction, the following claims of the '276 patent are deemed to be invalid:

1. A chemical compound or salt thereof having the formula (I):



(I)

wherein, at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.

2. A chemical compound according to claim **1**, wherein one or two of R_4, R_5, R_6, or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl) and bromine (Br).

3. A chemical compound according to claim **1**, wherein one or two of R_4, R_5, or R_6, are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl) and bromine (Br).

4. A chemical compound according to claim **1**, wherein two of R_4, R_5, and R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl) and bromine (Br).

5. A chemical compound according to claim **4**, wherein R_4 is halogenated, and wherein one of R_5, and R_6 is halogenated.

6. A chemical compound according to claim **4**, wherein R_5 is halogenated, and wherein one of R_4, and R_6 is halogenated.

7. A chemical compound according to claim **5**, wherein the halogen atoms are fluorine atoms.

8. A chemical compound according to claim **6**, wherein the halogen atoms are fluorine atoms.

9. A chemical compound according to claim **2**, wherein R_7 is a fluorine atom, and wherein one atom is halogenated.

10. A chemical compound according to claim **7**, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom.

11. A chemical compound according to claim **8**, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom.

12. A chemical compound according to claim **9**, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom.

13. A chemical compound according to claim **3**, wherein at least one of the halogen atoms is a chlorine atom.

14. A chemical compound according to claim **3**, wherein R_6 is a chlorine atom.

15. A chemical compound according to claim **14**, wherein R_5 is a fluorine atom.

16. A chemical compound according to claim **14**, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom.

17. A chemical compound according to claim **15**, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom.

18. A chemical compound according to claim **3**, wherein R_5 is a bromine atom, and the one atom is halogenated.

19. A chemical compound according to claim **18**, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom.

20. A chemical compound according to claim **2**, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group, and a (C_1-C_6)-acyl group.

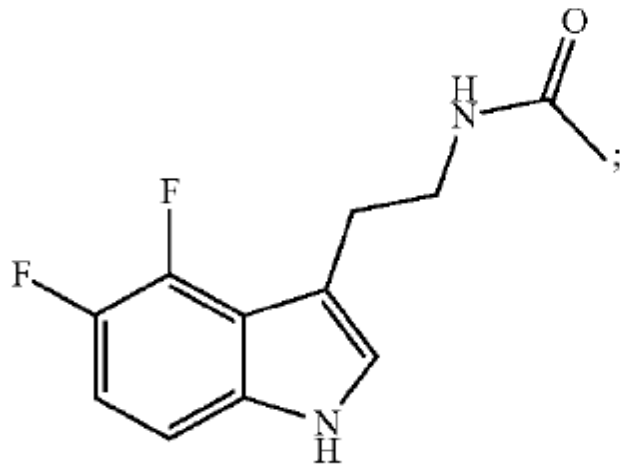
24. A chemical compound according to claim **16**, wherein R_{3a} and R_{3b} are each a (C_1-C_6)-alkyl group.

25. A chemical compound according to claim **17**, wherein R_{3a} and R_{3b} are each a (C_1-C_6)-alkyl group.

26. A chemical compound according to claim **19**, wherein R_{3a} and R_{3b} are each a (C_1-C_6)-alkyl group.

27. A chemical compound according to claim **1**, wherein the chemical compound is selected from the group consisting of compounds having formulas (V); (IX); (X); (XV); (XX); (XXI); (XXII); (XXIII); and (XXIV):

(V)



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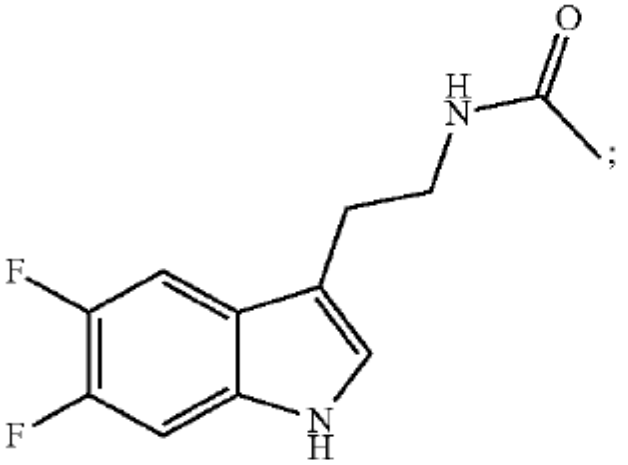
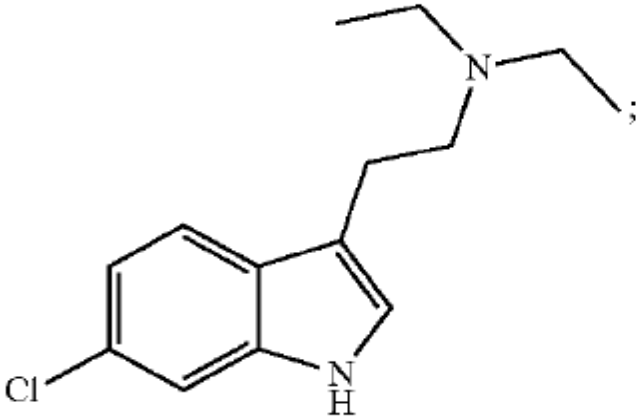
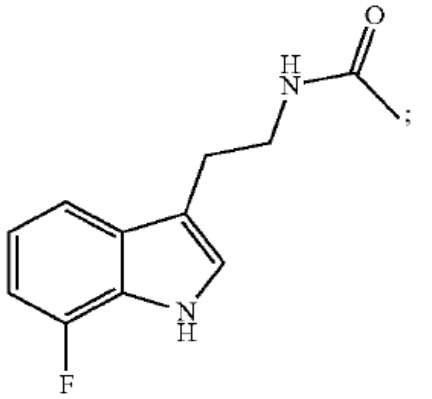


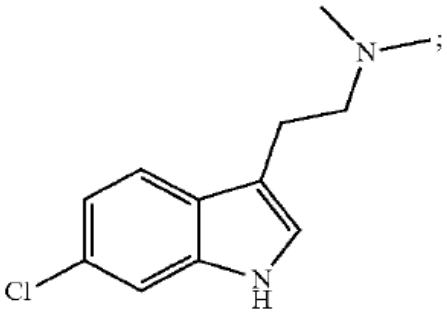
(X)



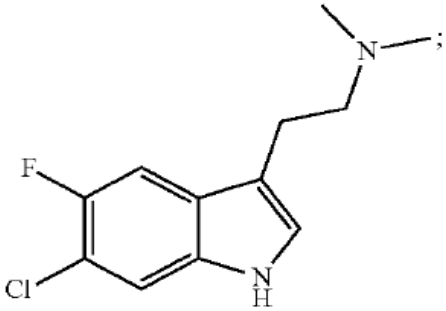
(XV)

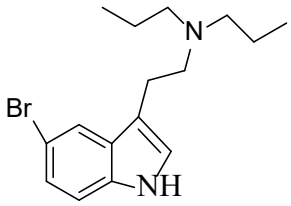


(XX)



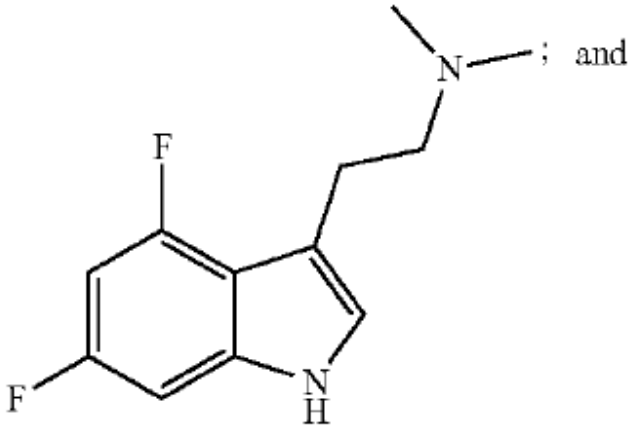
(XXI)





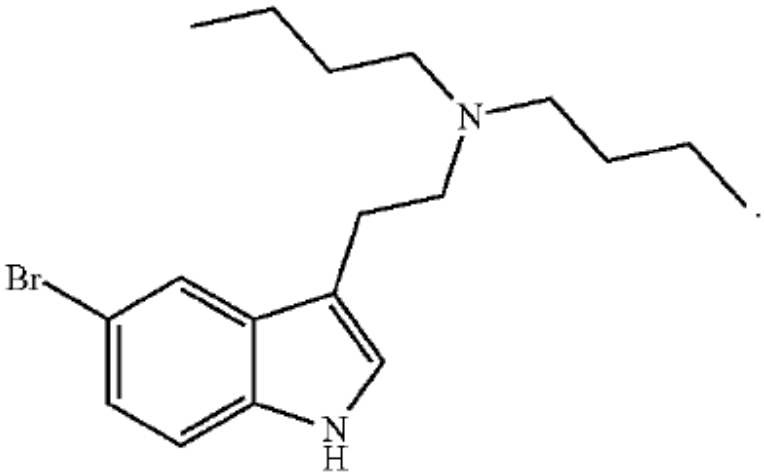
; (XXII)

(XXIII)



; and

(XXIV)



28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim **1**, together with a pharmaceutically acceptable excipient, diluent, or carrier.

29. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim **27**, together with a pharmaceutically acceptable excipient, diluent, or carrier.

III. STATEMENT OF PRECISE RELIEF REQUESTED

Claims 1-20 and 24-29 are unpatentable and should be canceled on several grounds:

Ground #	**Basis**
Ground I	Claims 1-20, 24, 26, and 28 are anticipated under 35 U.S.C. §§102.
Ground II	Subject matter in claim 27 is either anticipated under 35 U.S.C. §102 or rendered obvious under 35 U.S.C. §103.
Ground III	Claims 25 and 29 are rendered obvious under 35 U.S.C. §103.
Ground IV	Claim 1 is not enabled and is indefinite.

IV. CLAIM CONSTRUCTION

In a PGR proceeding, claim terms are to be construed using the standard under *Phillips v. AWH Corp.* 415 F.3d 1303 (Fed. Cir. 2005). In light of the intrinsic record and the state of the art as of the effective filing date of the '276 patent, a person of ordinary skill in the art would have understood the following claim terms to be construed as proposed below by Petitioner.

A. "Alky/O-Alkyl/Acyl

As used in claims 1, 2, 3, 4, the terms "alkyl" and "O-alkyl", and the term "acyl" in claim 1 is/are indefinite. Although these terms are commonly used in the field of organic chemistry, the skilled artisan understands these terms in general, but the upper limit of the number of carbon atoms in these terms is not defined in the specification or these specific claims.

The '276 patent defines these terms as follows:

> The term "alkyl", as used herein, refers to a straight and/or branched chain, saturated alkyl radical containing from one to "p" carbon atoms ("C_1-C_p-alkyl") and includes, depending on the identity of "p", methyl, ethyl, propyl, isopropyl

> n-butyl, s-butyl, isobutyl; t-butyl, 2,2-dimethylbutyl, n-pentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, n-hexyl and the like, where the variable p is an integer representing the largest number of carbon atoms in the alkyl radical. Alkyl groups further include hydrocarbon groups arranged in a chain having the chemical formula —C_nH_{2n+1}, including, without limitation, methyl groups (—CH_3), ethyl groups (—C_2H_5), propyl groups (—C_3H_7), and butyl groups (—C_4H_9).
> The term "O-alkyl," as used herein, refers to a hydrocarbon group arranged in a chain having the chemical formula —O—C_nH_{2n+1}. O-alkyl groups include, without limitation, O-methyl groups (—O—CH_3), O-ethyl groups (—O—C_2H_5) O-propyl groups (—O—C_3H_7) and O-butyl groups (—O—C_4H_9).
> The term "acyl," as used herein, refers to a carbon atom double bonded to an oxygen and single bonded to an alkyl group. The carbon atom further can be bonded to another entity. An acyl group can be described by the chemical formula: —C(═O)—C_nH_{2n+1}.

EX 1001, 24:19-42. Although the skilled artisan can provide examples of alkyl, such as methyl, ethyl, as defined, there is no upper limit to the number of carbon atoms present in the alkyl chain. As defined, the upper limit is "p" number of carbon atoms. Alternatively, the term alkyl is defined as C_nH_{2n+1}, but again, "n" is not defined. "A claim term construction that gives meaning to all of the terms in the claim is preferred over one that does not do so." *Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005). Moreover, it is not clear whether the upper limit in the term "alkyl" also applies to the "O-alkyl" and "acyl", as used in the '276 patent. "[W]hen an applicant uses different terms in a claim it is permissible to infer that he intended his choice of different terms to reflect a differentiation in meaning of these terms." *Innoval/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F3d 1111,1119 (Fed. Cir. 2004).

Accordingly, the term "alkyl," when used in any combination, must be consistently used. Based on the exemplification in the definitions of alkyl, the term "alkyl" when used alone or in combination, should be limited to 1-6 carbon atoms.

Moreover, the term "alkyl," based on the exemplification, should only consist of carbon and hydrogen atoms, and not include any other functional groups.

B. "Aryl"

The term "aryl" is also indefinite. The term "aryl" is defined in the '276 patent as follows:

> The term "aryl", as used herein, refers to a monocyclic, bicyclic or tricyclic aromatic ring system containing, depending on the number of atoms in the

> rings, for example, from 6 to 14 carbon atoms (C_6-C_{14}-aryl) or from 6 to 10 carbons (C_6-C_{10}-aryl), and at least 1 aromatic ring and includes phenyl, naphthyl, anthracenyl, 1,2-dihydronaphthyl, 1,2,3,4-tetrahydronaphthyl, fluorenyl, phenanthrenyl, biphenylenyl, indanyl, indenyl and the like.

EX. 1001, 24:43-50. Just as with "alkyl", there is no upper limit to the number of carbon atoms. The comments regarding the lack of clarity of "alkyl", are also applicable for this term. Thus, without any upper limit of the carbon atoms, the term "aryl" is not limited to any particular length, size, or substitution.

Based on the exemplification, the term "aryl" should be limited to monocyclic, bicyclic, tricyclic aromatic ring system containing 6 to 14 ring carbon atoms and at least one aromatic ring. From the exemplification, the rings are fused, and if there is more than 1 ring, the other rings can be non-aromatic. However, the term, as defined, excludes heterocyclic or heteroaryl.

C. "…wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom".

There is ambiguity in this phrase with respect to claims 12, 16, 17, and 18. Claim 12 is dependent on claim 9, wherein R_7 is defined as fluorine. When claim 12 refers to claim 9 and recites that each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom, it appears that claim 12 is ignoring the definition of R_7 being fluorine. Since R_7 is fluorine, it cannot be non-halogenated and thus the recitation in claim 12 can be construed as inconsistent with the language in claim 9. Similarly, claim 14 defines R_6 as a chlorine atom, but claim 16 (dependent on claim 14) recites that each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom; it appears that claim 14 is ignoring that R_6 is chlorine. The same comment is applicable to claim 17, which is dependent on claim 14 and claim 15. Claim 14 defines R_6 as chlorine and claim 15 recites R_5 as fluorine, but claim 17 recites that each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom. Again, the recitation in claim 17 is confusing, but as defined in claims 14 and 15 from which claim 17 is dependent, R_5 and R_6 are already defined. It is unclear what the terminology patentee is referring to with respect to the variables R_5 and R_6. Finally, claim 18 defines R_5 as bromine, but claim 19 recites that each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom. The same comment as indicated above is also applicable.

Accordingly, with respect to claim 12, the claim should be construed that the recitation regarding R_7 is superfluous; with respect to claim 16, the claim should be construed that the

recitation regarding R_6 is superfluous; with respect to claim 17, the claim should be construed that the recitation regarding R_5 and R_6 is superfluous; and that with respect to claim 19, the claim should be construed that the recitation regarding R_5 is superfluous.

V. ARGUMENTS

A. ANTICIPATION

Subject matter in claims 1-20, 24, 26, and 28 are anticipated under 35 U.S.C. §102(a), which reads in relevant part:

> (a) NOVELTY: PRIOR ART- A person shall be entitled to a patent unless-
>
> (1) the claimed invention was patented, described in a printed publication… before the effective filing date of the invention; or
> (2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b). in which the patent or application…names another inventor and was effectively filed before the effective filing of the claimed invention.

The underlying application of the '276 patent is a continuation of USSN 17/903,080 filed on Sept. 6, 2022, now US Patent No. 11,998,557, which is a continuation of international application having serial number PCT/CA2021/051209, filed on September 1, 2021, and claiming priority of provisional application USSN 63/073,104, filed on September 1, 2020. Thus, the effective filing date of the claimed subject matter in the '276 patent is no earlier than September 1, 2020. Accordingly, relevant patents/applications and other publications that were published prior to September 1, 2020 are considered prior art to the '276 patent pursuant to 35 U.S.C. §102(a)(1) and U.S. Patents or U.S Patent Application Publications applications that have an effective filing date prior to September 1, 2020, by inventors other than Hagel et al. are prior art to the '276 patent pursuant to 35 U.S.C. §102 (a)(2).

Anticipation of a claim requires that a single source contain all of the elements of the claim. *See, Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). Further, the "way in which the elements are arranged or combined in the claim must itself be disclosed, either expressly or inherently, in an anticipatory reference." *Therasense, Inc. v. Becton, Dickinson & Co.,* 593 F.3d 1325, 1332 (Fed. Cir. 2010).

A compound or composition of matter is anticipated if a single prior art reference places the compound or composition of matter in the possession of the public. *In re Brown*, 329 F.2d 1006, 1011 (CCPA 1964). This single prior art reference must "clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing, and combining various disclosures…" *In re Arkley*, 455 F.2d 586.587 (CCPA 1972).

"In chemical compounds, a single prior art species within the patent's claimed genus reads on the generic claim and anticipates." *See, Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1346 (Fed. Cir. 1999) (citing *In re Gosteli*, 872. F.2d 1008, 1010 (Fed. Cir. 1989). Regardless if the prior art reference contains other species or teachings, this premise still holds true. *See, In re Sivarmakrishnan*, 673 F.2d 1383 (CCPA 1982).

Thus, as long as the prior art reference discloses a species of a later claimed genus containing that species, the prior art reference is deemed to anticipate the claim. *In re Gosteli, supra*.

The following pages discuss relevant references that disclose one or more species of the genus claim and dependent claims of the '276 patent. Tables are provided for convenience. The left-hand side of the table lists the claims of the '276 patients that are relevant with respect to the species of the prior art; the right-hand side of the table identifies the portion of the claim of the left side of the table which is anticipated by the species of the prior art listed hereinbelow.

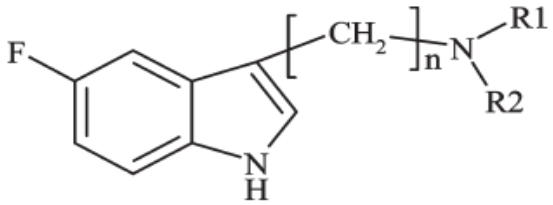
B. PRIOR ART REFERENCES

1. Soubhye et al., J. Med. Chem. 2010, 53, 8747-8759 (EX 1003)

This is an article (hereinafter referred to as "Soubhye et al."), which was published in 2010, which is more than a year prior to the earliest priority date of the '276 patent, which is September 1, 2020. Thus, it qualifies as prior art.

It discloses 3-(aminoalkyl)-5-fluoroindole analogues that were designed and synthesized to investigate the structure-based docking of 5-fluorotryptamine, which is known as an inhibitor of myeloperoxidase (MPO). It discloses 5-chlorotryptamine (identified therein as compound 3) and 5-fluorotryptamine (identified therein as compound 4) and synthesized and tested the following compounds:

Table 1. IC_{50} Values for the Inhibition of MPO, Predicted Free Energies of Binding Obtained from Docking Experiments[a]

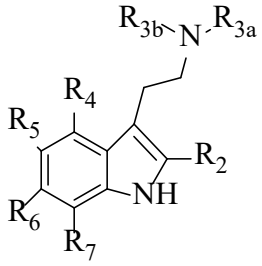


no.	*n*	R_1	R_2	IC_{50} (μM)	ΔG (kcal/mol)
6	1	H	H	0.9 ± 0.3	−5.3
7	1	C_2H_5	C_2H_5	0.2 ± 0.2	−6.3
8	1	*N*-methylpiperazinyl		1.0 ± 0.1	−7.3
4	2	H	H	0.20 ± 0.03	−6.5
16	2	CH_3	H	0.20 ± 0.02	−6.6
17	2	C_2H_5	H	0.3 ± 0.1	−6.8
18	2	C_3H_7	H	0.80 ± 0.02	−6.6
19	2	C_4H_9	H	1.03 ± 0.08	−6.5
20	2	CH_3	CH_3	0.09 ± 0.06	−7.0
21	2	C_2H_5	C_2H_5	0.16 ± 0.08	−6.3
22	2	pyrrolidinyl		0.04 ± 0.03	−6.8
23	2	*N*-methylpiperazinyl		0.2 ± 0.1	−7.7
15	3	H	H	0.050 ± 0.008	−6.4
24	3	CH_3	H	0.2 ± 0.2	−6.7
25	3	C_2H_5	H	0.3 ± 0.1	−6.6
26	3	C_3H_7	H	0.17 ± 0.08	−7.5
27	3	C_4H_9	H	1.5 ± 0.5	−6.8
28	3	CH_3	CH_3	0.13 ± 0.09	−5.7
29	3	C_2H_5	C_2H_5	0.35 ± 0.09	−7.0
30	3	pyrrolidinyl		0.32 ± 0.01	−7.5
31	3	*N*-methylpiperazinyl		0.35 ± 0.06	−8.5
34	4	H	H	0.015 ± 0.004	−6.6
41	5	H	H	0.008 ± 0.002	−6.4
48	6	H	H	0.26 ± 0.01	−5.9

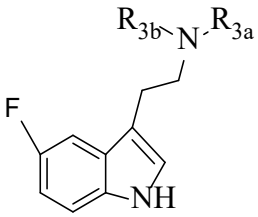
[a] Compounds are classified first following the length of the side chain and the substituents, then, respectively, according the mono- or disubstitution of the amino group. The IC_{50} value is the mean ± SD of 3 independent experiments.

The following tables compare the compounds described in Soubhye et al. on the right-hand side thereof with the language in the claims in the '276 patent reproduced hereinbelow on the left-hand side thereof. Numbers in the right-hand column refer to the compound numbers in Soubhye et al.

Table 2(a)



(I)

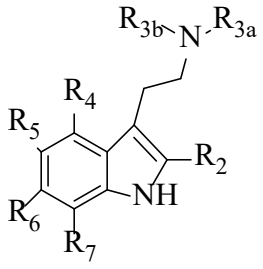


US 12,138,276	Soubhye et al.
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	4. R_{3a} is H and R_{3b} is H; R_5 is halo (R_5 is F); R_2, R_4, R_6, and R_7 are H. 16. R_{3a} is alkyl (CH_3) and R_{3b} is H; R_5 is halo (R_5 is F); R_2, R_4, R_6, and R_7 are H. 17. R_{3a} is alkyl (C_2H_5) and R_{3b} is H; R_5 is halo (R_5 is F); R_2, R_4, R_6, and R_7 are H. 18. R_{3a} is alkyl (C_3H_7) and R_{3b} is H; R_5 is halo (R_5 is F); R_2, R_4, R_6, and R_7 are H. 19. R_{3a} is alkyl (C_4H_9) and R_{3b} is H; R_5 is halo (R_5 is F); R_2, R_4, R_6, and R_7 are H. 20. R_{3a} is alkyl (CH_3) and R_{3b} is alkyl (CH_3); R_5 is halo (R_5 is F); R_2, R_4, R_6, and R_7 are H. 21. R_{3a} is alkyl (C_2H_5) and R_{3b} is alkyl (C_2H_5); R_5 is halo (R_5 is F); R_2, R_4, R_6, and R_7 are H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	4, 16.-21. R_5 is halo (R_5 is F); R_4, R_6 and R_7 are H.

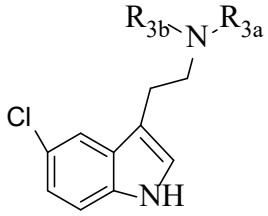
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	4, 16.-21. R_5 is halo (R_5 is F); R_4 and R_6 are H.
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	4. R_{3a} is H and R_{3b} is H. 16. R_{3a} is (C_1-C_6)-alkyl (R_{3a} is CH_3) and R_{3b} is H. 17. R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_2H_5) and R_{3b} is H. 18. R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is H. 19. R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_4H_9) and R_{3b} is H. 20. R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} is CH_3 and R_{3b} is CH_3). 21. R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} is C_2H_5 and R_{3b} is C_2H_5).

Thus, Soubhye et al. anticipates the subject matter of claims 1-3, and 20 under 35 U.S.C. §102(a)(1).

Table 2(b)



(I)



US 12,138,276	Soubhye et al.
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and	3. R_{3a} and R_{3b} are hydrogen, R_5 is halo (R_5 is Cl); R_2, R_4, R_6 and R_7 are H.

R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	R_5 is halo (R_5 is Cl).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	R_5 is halo (R_5 is Cl).
13. A chemical compound according to claim 3, wherein at least one of the halogen atoms is a chlorine atom.	R_5 is halo (R_5 is Cl).
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	R_{3a} and R_{3b} are H.

Thus, compound 3 of Soubhye anticipates the subject matter of clams 1-3, 13, and 20 under 35 U.S.C. §102(a)(1).

Therefore, combining the results of the two tables, EX 1003 anticipates the subject matter of claims 1-3, 13 and 20.

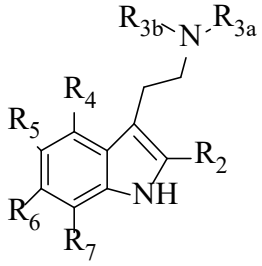
2. Kalir et al., Journal of Medicinal Chemistry, 9(3), 341-344 (May 1966) (EX 1004)

Kalir et al. (“ Kalir et al.”) published in 1966, is prior to the earliest priority date of September 1, 2020, of the ‘276 patent. Accordingly, Kalir et al. is prior art to the ‘276 patent.

Kalir et al. disclose the preparation of various 3-(N-alkylaminoalkyl-α-methyl)indoles. They found the introduction of a methyl group into the nitrogen atom of the amine resulted in a compound that caused the arousal of the motor activity in reserpinized mice in much shorter time relative to the compound without the additional methyl group. They also found that the introduction of a higher alkyl group or a second methyl group caused a decrease in physiological activity. They further teach that elongation in the aliphatic group on the tryptamine caused a complete loss of action.

The relevant compounds with respect to the teachings of the ‘276 patent are indicated below in the following tables. The following tables compare the compounds described in this article on the right-hand side thereof with the language in the claims in the ‘276 patent reproduced hereinbelow on the left-hand side thereof. Numbers in the right-hand column refer to the compound numbers in the article.

Table 3(a)



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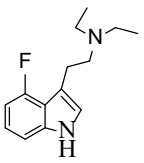
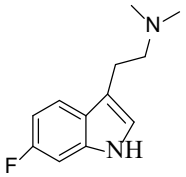


15



20

US 12,138,276 Kalir et al.

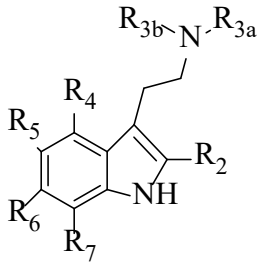
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	15. R_4 is halo (R_4 is F); R_2, R_5, R_6 and R_7 are hydrogen; R_{3a} and R_{3b} are both alkyl groups (R_{3a} and R_{3b} are both ethyl). 20. R_4 is halo (R_4 is F); R_2, R_5, R_6 and R_7 are hydrogen; R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both methyl).
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	15. R_4 is halo (R_4 is F). 20. R_4 is halo (R_4 is F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is	15. R_4 is halo (R_4 is F). 20. R_4 is halo (R_4 is F).

selected from fluorine (F), chlorine (Cl), and bromine (Br).	
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	15. R_{3a} and R_{3b} are both (C_1-C_6)-alkyl groups (R_{3a} and R_{3b} are both ethyl). 20. R_{3a} and R_{3b} are both (C_1-C_6)-alkyl groups (R_{3a} and R_{3b} are both methyl).
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	15. "Pharmacological Findings. General Procedure…" on page 342. 20. "Pharmacological Findings. General Procedure…" on page 342

Thus, the compounds from Kalir et al. depicted in the above table anticipate the subject matter in claims 1, 2, 3, 20 and 28 of the '276 patent under 35 U.S.C. §102(a)(1).

Kalir et al. also disclose compounds 18 and 19 depicted below in Table 3b.

Table (3b)



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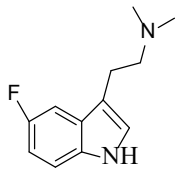
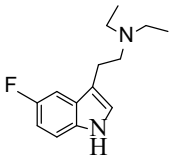


18



19

US 12,138,276	Kalir et al.
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and	18. R_5 is halo (F); R_2, R_4, R_6 and R_7 are hydrogen; R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both methyl). 19. R_5 is halo (F); R_2, R_4, R_6 and R_7 are hydrogen; R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both ethyl).

R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	
2. 2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	18. R_5 is halo (F). 19. R_5 is halo (F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	18. R_5 is halo (F). 19. R_5 is halo (F).
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	18. R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both methyl). 19. R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both ethyl).
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	18. "Pharmacological Findings. General Procedure…" on page 342. 19. "Pharmacological Findings. General Procedure…" on page 342

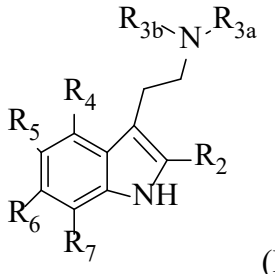
Accordingly, the subject matter in Kalir et al. anticipate claims 1-3, 20, and 28 of the '276 patent under 35 U.S.C. §102(a)(1)

3. Pelchowicz et al., Journal of the Chemical Society, pp.5418-5421 (June 1961) (EX 1005)

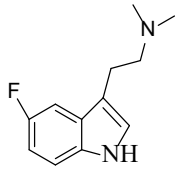
Pelchowicz et al. ("Pelchowicz et al.") was published in 1961, which is prior to the earliest priority date of September 1, 2020, of the '276 patent. Accordingly, Pelchowicz et al. is prior art to the '276 patent.

Pelchowicz et al. disclose the syntheses of various 5-fluoroindoles. The relevant compounds are indicated in Table 4 below on the right-hand side. They are 6-fluoro-N,N-dimethyltryptamine, indicated as compound "a", and N,N-diethyl-5-fluorotryptamine, indicated as compound "b" in the following table. The table compares these compounds described in Pelchowicz et al. on the right-hand side thereof with the language in the claims in the '276 patent reproduced hereinbelow on the left-hand side thereof.

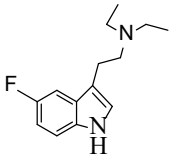
Table 4



(I)



(a)



(b)

US 12,138,276	Pelchowicz et al.
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	(a) R_5 is halo (F); R_2, R_4, R_6 and R_7 are hydrogen; R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both methyl). (b) R_5 is halo (F); R_2, R_4, R_6 and R_7 are hydrogen; R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both ethyl).
2. 2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a) R_5 is halo (F). (b) R_5 is halo (F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a) R_5 is halo (F). (b) R_5 is halo (F).
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(a) R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both methyl). (b) R_{3a} and R_{3b} are both alkyl group (R_{3a} and R_{3b} are both ethyl).

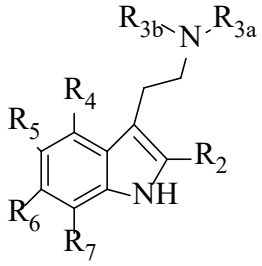
Accordingly, Pelchowicz et al. disclose species which anticipate claims 1-3 and 20 of the '276 patent under 35 U.S.C. §102(a)(1).

4. EP 2,686,119 (EX 1006)

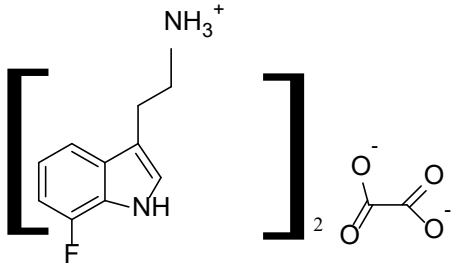
This EPO patent application ("EP '119") published on January 8, 2014, is prior to the earliest priority date of September 1, 2020, of the '276 patent. Accordingly, EP '119 is prior art to the '276 patent.

One of the compounds disclosed therein is 3-(2-aminoethyl)-7-fluoro-1H-indole oxalate (26), which is depicted on the right side of Table 5 below. Table 5 compares this compound with the language in the relevant claims in the '276 patent reproduced hereinbelow on the left-hand side of Table 5.

Table 5



(I)



26

US 12,138,276	EP 2682119
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_7 is halo (R_7 is F); R_2, R_4, R_5, and R_6 are H; R_{3a} and R_{3b} are hydrogen.
2. A chemical compound according to claim **1,** wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_7 is halo (R_7 is F).

9. A chemical compound according to claim **2,** wherein R_7 is a fluorine atom, and wherein one atom is halogenated.	Salt, wherein R_7 is halo (R_7 is F).
12. A chemical compound according to claim **9**, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom.	Salt, wherein R_7 is halo (R_7 is F) and R_2, R_4, R_5, and R_6 are hydrogen.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Salt, wherein R_{3a} and R_{3b} are hydrogen.

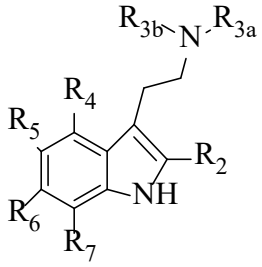
Accordingly, this compound in EP '119 anticipates claims 1, 2, 9, 12, and 20 of the '276 patent under 35 U.S.C. §102(a)(1) and 102(a)(2).

5. US 3,780,063 (EX 1007)

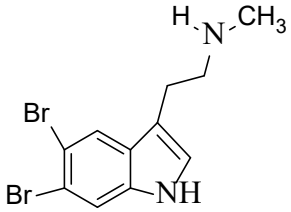
US 3,780,063 ("US '063") issued on Dec. 18, 1973, is prior to the earliest priority date of September 1, 2020, of the '276 patent. Accordingly, US '063 is prior art to the '276 patent.

US '063 describes two compounds isolated from a marine sponge as *Polyfibrospongia maynardii*. These compounds are 5,6-dibromo-3-(2-methylaminoethyl)indole and 3-(2-aminoethyl)-5,6-dibromoindole. These compounds are depicted on the right side of Table 8, labeled as (a) and (b) respectively. The following table compares these compounds with the language in the relevant claims in the '276 patent reproduced hereinbelow on the left-hand side of Table 6.

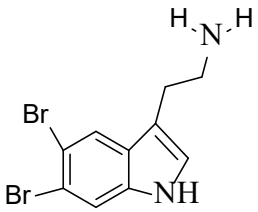
Table 6



(I)



(a)



(b)

US 12,138,276	US 3,780,063
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	(a)R_5 and R_6 are halo (R_5 and R_6 are Br); R_{3a} is alkyl (R_{3a} is CH_3) and R_{3b} is H; R_2, R_4 and R_7 are H. (b)R_5 and R_6 are halo (R_5 and R_6 are Br); R_{3a} is H and R_{3b} is H; R_2, R_4 and R_7 are H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a)R_5 and R_6 are halo (R_5 and R_6 are Br). (b)R_5 and R_6 are halo (R_5 and R_6 are Br).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a)R_5 and R_6 are halo (R_5 and R_6 are Br). (b)R_5 and R_6 are halo (R_5 and R_6 are Br).
4. A chemical compound according to claim 1 wherein two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a)R_5 and R_6 are halo (R_5 and R_6 are Br). (b)R_5 and R_6 are halo (R_5 and R_6 are Br)
6. A chemical compound according to claim 4 wherein R_5 is halogenated, and wherein one of R_4, and R_6 is halogenated.	(a)R_5 and R_6 are halo (R_5 and R_6 are Br). (b)R_5 and R_6 are halo (R_5 and R_6 are Br).

20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(a)R_{3a} is alkyl (C_1-C_6)-alkyl (R_{3a} is CH_3) and R_{3b} is H. (b)R_{3a} is H and R_{3b} is H.

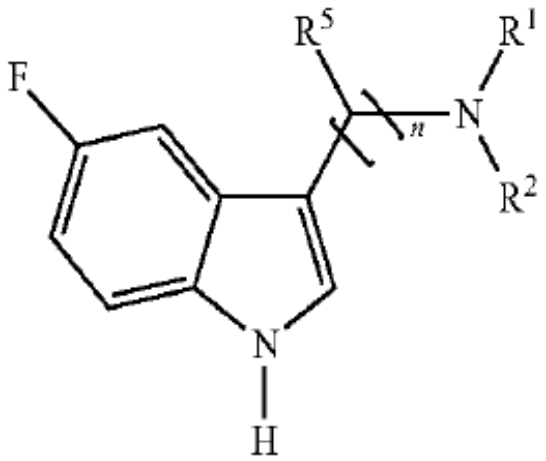
Accordingly, these compounds in US '063 anticipate the subject matter in claims 1, 2, 4, 6 and 20 of the '276 patent under 35 U.S.C. §102(a)(1) and 102(a)(2)

6. US 2012/0122948 (EX 1008)

US 2012/0122948 ("US '948") was published on May 17, 2012, which is prior to the earliest priority date of September 1, 2020, of the '276 patent. Accordingly, US '948 is prior art to the '276 patent.

It discloses compounds of the formula:

(Ia)



or pharmaceutically acceptable salt thereof wherein

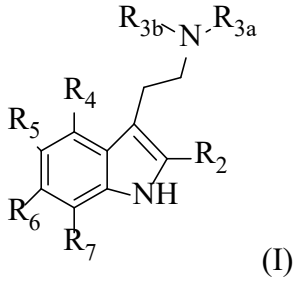
n is an integer between 2 and 10,

R^1 and R^2 independently represent a substituent selected from the group consisting of hydrogen, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl and aminoalkyl or R^1 and R^2 are taken together with the nitrogen atom to which they are attached to form a four to ten-membered heterocycle,

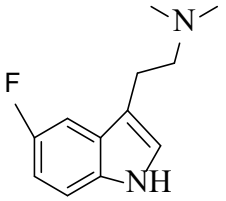
R^5 represents independently in each of the n units a substituent selected from the group consisting of hydrogen, C_1-C_6 alkyl, halogen, alkoxy, aminoalkyl and alkylamino, provided that 5-fluorotryptamine is excluded.

This compound of Formula I is allegedly useful for the treatment or prophylaxis of diseases or disorders in which the activity of the enzyme myeloperoxidase is beneficial, such as, neuroinflammatory diseases, such as, multiple sclerosis, Alzheimer's disease, Parkinson's disease, pain (see paragraph [053]). It also discloses various compounds, such as N,N-dimethyl-3-(2-aminoethyl)-5-fluoro-[1H]-indole in Example 3 thereof and N,N-diethyl-3-(2-aminoethyl)-5-fluoro-[1H]-indole in Example 5, thereof. These latter two compounds are depicted on the right side of Table 7, identified therein as Ex. 3 and Ex. 5, respectively. Table 7 shows how these compounds fall within the scope of the language of various claims of the '276 patent reproduced hereinbelow on the left-hand side of Table 7.

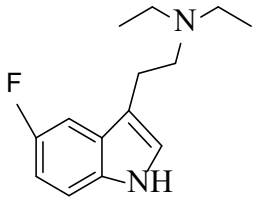
Table 7



(I)



Ex3



Ex5

US 12,138,276	US 2012/0122948
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Ex 3: R_5 is halo (R_5 is F); R_{3a} and R_{3b} are alkyl (R_{3a} and R_{3b} are CH_3); R_2, R_4, R_6 and R_7 are H. Ex 5: R_5 is halo (R_5 is F); R_{3a} and R_{3b} are alkyl (R_{3a} and R_{3b} are C_2H_5); R_2, R_4, R_6 and R_7 are H.

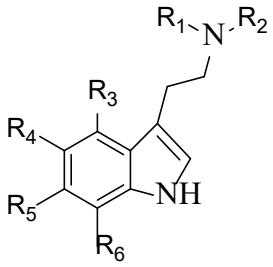
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Ex 3: R_5 is halo (R_5 is F). Ex 5: R_5 is halo (R_5 is F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Ex 3: Ex 3: R_5 is halo (R_5 is F). Ex 5: R_5 is halo (R_5 is F).
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Ex 3: R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} and R_{3b} are CH_3). Ex 5: R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} and R_{3b} are C_2H_5).
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	See ¶ 15 of US 2012/0122948

Accordingly, this example in US '948 anticipates the subject matter of claims 1-3, 20, and 28 of the '276 patent under 35 U.S.C. §102(a)(1) and 102(a)(2).

7. USSN 62/978, 075 (EX 1009)

USSN 62/978,075 ("USSN '075") is a provisional application to which US 11,440,879 (US '879") (**EX 1010**) claims priority. USSN '075 was filed on February 18, 2020, thus US '879 has an effective filing date of February 18, 2020, for subject matter described in USSN '075. Inasmuch as USSN '075 was filed prior to the earliest effect filing date of the '276 patent, which is September 1, 2020, pursuant to 35 U.S.C. §102(a)(2), it is considered prior art to the '276 patent to the extent that the subject matter of USSN '075 is described in US '879.

USSN '075 as well as US '879 describes, *inter alia*, a tryptamine compound of the formula:



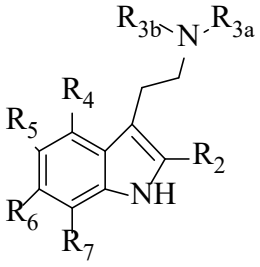
wherein

R_1, R_2 = Me, Et, nPr, iPr, cyclopropyl, allyl, isobutyl, cyclopropylmethyl;

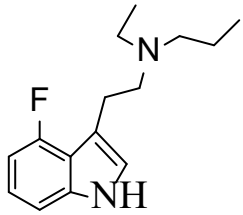
R_3-R_7=H, F, Cl, Br, I, CF_3, Me;

USSN '075 describes several species, which are indicated in the following Tables 8(a)-8(f). The right-hand side of each of the tables shows how each of the species described therein fall within the scope of the language of relevant claims of the '276 patent, which is described on the left side of each of the tables.

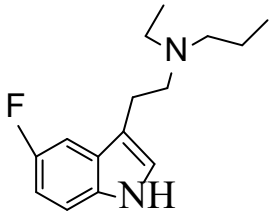
Table 8(a)



(I)



(a)



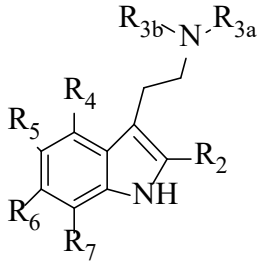
(b)

US 12,138,276	USSN 62/978,075
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and	(a) R_4 is halo (R_4 is F); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_5, R_6, R_7 are H. (b)R_5 is halo (R_5 is F); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_4, R_6, R_7 are H.

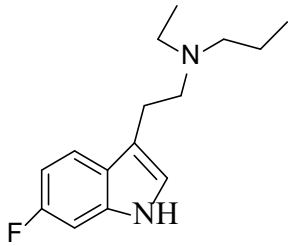
R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a)R_4 is halo (R_4 is F). (b)R_5 is halo (R_5 is F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a)R_4 is halo (R_4 is F). (b)R_5 is halo (R_5 is F).F
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(a)R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5) (b) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5).
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	(a)Page 16, line 25-page 17, line 21 (b) Page 16, line 25-page 17, line 21

Thus, claims 1-3, 20 and 28 of the ‘276 patent are anticipated by this teaching in USSN ‘075 under 35 U.S.C. §102(a)(2).

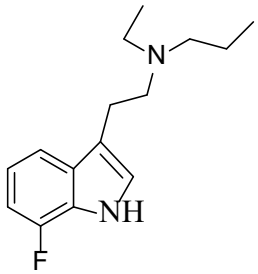
Table 8(b)



(I)



(c)



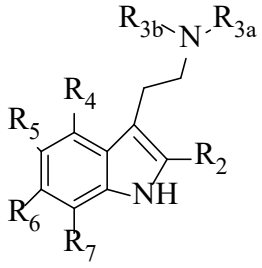
(d)

US 12,138,276	USSN 62/978,075
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-	(c) R_6 is halo (R_6 is F); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_4, R_5, R_7 are H.

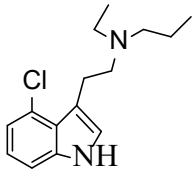
halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	(d) R_7 is halo (R_7 is F); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_4, R_5, R_6, are H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(c) R_6 is halo (R_6 is F). (d) R_7 is halo (R_7 is F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(c) R_6 is halo (R_6 is F).
9. A chemical compound according to claim 2 wherein R_7 is a fluorine atom, and wherein one atom is halogenated.	(d) R_7 is halo (R_7 is F).
12. A chemical compound according to claim 9, wherein each non-halogenated R_2, R_4, R_5, R_6, or R_7 is a hydrogen atom.	(d) R_2, R_4, R_5, and R_6, are hydrogen atoms.
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(c) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5). (d) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5).
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	(c)Page 16, line 25-page 17, line 21 (d) Page 16, line 25-page 17, line 21

Thus, the subject matter of claims 1-3, 9, 12, 20, and 28 of the ‘276 patent is anticipated by the aforementioned compounds in USSN ‘075 under 35 U.S.C. §102(a)(2).

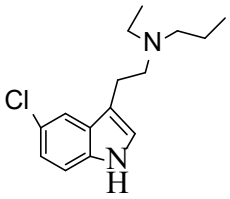
Table 8(c)



(I)



(a)



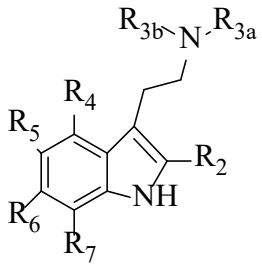
(b)

US 12,138,276	USSN 62/978,075
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	(a) R_4 is halo (R_4 is Cl); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_5, R_6, R_7 are H. (b)R_5 is halo (R_5 is Cl); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_4, R_6, R_7 are H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a) R_4 is halo (R_4 is Cl). (b) R_5 is halo (R_5 is Cl).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a) R_4 is halo (R_4 is Cl). (b) R_5 is halo (R_5 is Cl).
13.A chemical compound according to claim 3, wherein at least one of the halogen atoms is a chlorine atom.	(a) R_4 is halo (R_4 is Cl). (b) R_5 is halo (R_5 is Cl).
20. A chemical compound according to claim 2 wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(a) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (C_2H_5). (b) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5).

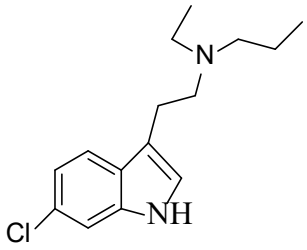
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	(a)Page 16, line 25-page 17, line 21 (b) Page 16, line 25-page 17, line 21

Consequently, this teaching of USSN '075 anticipates claims 1-3, 13, 20 and 28 of the '276 patent under 35 U.S.C. §102(a)(2).

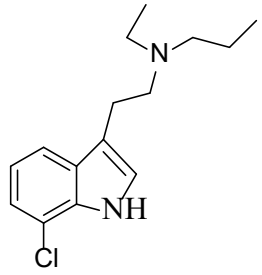
Table 8(d)



(I)



(c)



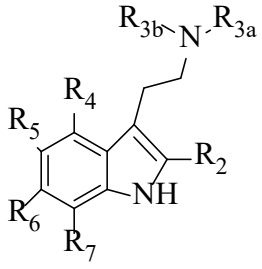
(d)

US 12,138,276	USSN 62/978,075
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	(c) R_6 is halo (R_6 is Cl); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_4, R_5, R_7 are H. (d)R_7 is Cl; R_{3a} is alkyl (C_3H_7) and R_{3b} is alkyl (C_2H_5); R_2, R_4, R_5, R_6, are H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(c) R_6 is halo (R_6 is Cl). (d) R_7 is halo (R_7 is Cl).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is	(c) R_6 is halo (R_6 is Cl). (d) R_7 is halo (R_7 is Cl).

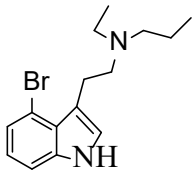
selected from fluorine (F), chlorine (Cl), and bromine (Br).	
13. A chemical compound according to claim 3, wherein at least one of the halogen atoms is a chlorine.	(c) R_6 is halo (R_6 is Cl). (d) R_7 is halo (R_7 is Cl).
14. A chemical compound according to claim 3, wherein R_6 is a chlorine atom.	(c) R_6 is Cl.
16. A chemical compound according to claim 14, wherein each non-halogenated R_2, R_4, R_5, R_6, or R_7, is a hydrogen atom.	(c) R_2, R_4, R_5, and R_7, are hydrogen atoms.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(c) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5). (d) R_{3a} is alkyl (C_3H_7) and R_{3b} is alkyl (C_2H_5)
24. A chemical compound according to claim 16, wherein R_{3a} and R_{3b} are each a (C_1-C_6) alkyl group.	(c) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5). (d) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5.
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	(c)Page 16, line 25-page 17, line 21 (d) Page 16, line 25-page 17, line 21

Therefore, claims 1-3, 13, 14, 16, 20, 24, and 28 of the ‘276 patent are anticipated by these compounds in USSN ’075 under 35 U.S.C. §102(a)(2).

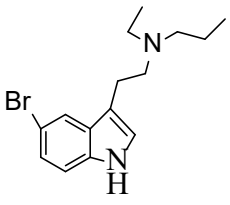
Table 8(e)



(I)



(a)



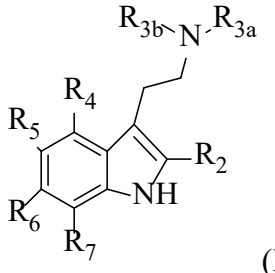
(b)

US 12,138,276	USSN 62/978,075
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	(a) R_4 is halo (R_4 is Br); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_5, R_6, R_7 are H. (b) R_5 is halo (R_5 is Br); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_4, R_6, R_7 are H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a) R_4 is halo (R_4 is Br). (b) R_5 is halo (R_5 is Br).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a) R_4 is halo (R_4 is Br). (b) R_5 is halo (R_5 is Br).
18. A chemical compound according to claim 3, wherein R_5 is a bromine atom, and one atom is halogenated.	(b) R_5 is Br
19. A chemical compound according to claim 18, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7 is a hydrogen atom.	(b) R_2, R_4, R_6 and R_7 are hydrogen.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(a) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5). (b) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5).
26. A chemical compound according to claim 19, wherein R_{3a} and R_{3b} are each a (C_1-C_6) alkyl group.	(a) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5). (b) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5).
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1,	(a) Page 16, line 25-page 17, line 21 (b) Page 16, line 25-page 17, line 21

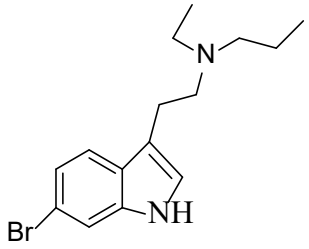
together with a pharmaceutically acceptable excipient, diluent, or carrier.	

Accordingly, these compounds in USSN '075 anticipate claims 1-3, 18-20, 26 and 28 of the '276 patent under 35 U.S.C. §102(a)(2).

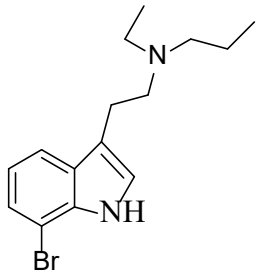
Table 8(f)



(I)



(c)



(d)

US 12,138,276	USSN 62/978,075
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	(c) R_6 is halo (R_6 is Br); R_{3a} is alkyl (R_{3a} is C_3H_7) and R_{3b} is alkyl (R_{3b} is C_2H_5); R_2, R_4, R_5, R_7 are H. (d) R_7 is halo (R_7 is Br); R_{3a} is alkyl (C_3H_7) and R_{3b} is alkyl (C_2H_5); R_2, R_4, R_5, R_6, are H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(c) R_6 is halo (R_6 is Br). (d) R_7 is halo (R_7 is Br).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(c) R_6 is halo (R_6 is Br). (d) R_7 is halo (R_7 is Br).

20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(c) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5). (d) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5).
26. A chemical compound according to claim 19, wherein R_{3a} and R_{3b} are each a (C_1-C_6)-alkyl group.	(c) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5). (d) R_{3a} is (C_1-C_6)-alkyl (R_{3a} is C_3H_7) and R_{3b} is (C_1-C_6)-alkyl (R_{3b} is C_2H_5).
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	(c)Page 16, line 25-page 17, line 21 (d)Page 16, line 25-page 17, line

Accordingly, these compounds in USSN ‘075 anticipate claims 1-3, 20, 26 and 28 of the ‘276 patent under 35 U.S.C. §102(a)(2).

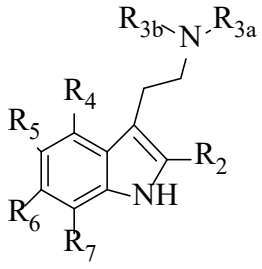
Therefore, the teachings in USSN ‘075 invalidate claims 1-3, 9, 12-14, 16, 18-20, 24, 26, and 28 of the ‘276 patent under 35 U.S.C. §102(a)(2).

8. US 2012/0029010 (EX 1011)

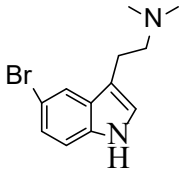
US 2012/0029010 (“US ‘010”) published on February 2, 2012, which is prior to the earliest priority date of September 1, 2020, of the ‘276 patent. Accordingly, US ‘010 is prior art to the ‘276 patent.

US ‘010 teaches the isolation of various compounds, such as 5,6-dibromo-N,N-dimethyltryptamine and 5-bromo-N,N-dimethyltryptamine, from sponges and uses thereof. The former compound is useful in treating neurological conditions, such as depression, while the latter compound is a sedative. These two compounds fall within the scope claims of the ‘276 patent, as shown in the following table. The right-hand side of each of the table shows how each species described therein falls within the scope of the language of relevant claims of the ‘276 patent, which is described on the left-hand side of each of the tables.

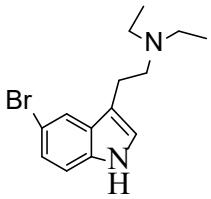
Table 9



(I)



(a)



(b)

US 12,138,276	US 2012/0029010
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	(a) R_5 is halo (R_5 is Br); R_{3a} and R_{3b} are alkyl (R_{3a}=R_{3b}=CH_3); R_2, R_4, R_6, R_7 are H. (b) R_5 is halo (R_5 is Br); R_{3a} and R_{3b} are alkyl (R_{3a}=R_{3b}=C_2H_5); R_2, R_4, R_6, R_7 are H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a) R_5 is halo (R_5 is Br). (b) R_5 is halo (R_5 is Br).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	(a) R_5 is halo (R_5 is Br). (b) R_5 is halo (R_5 is Br).
18. A chemical compound according to claim 3, wherein R_5 is a bromine atom, and one atom is halogenated.	(a) R_5 is Br. (b) R_5 is Br.
19. A chemical compound according to claim 18, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7 is a hydrogen atom.	(a) R_2, R_4, R_6, R_7 are H. (b) R_2, R_4, R_6, R_7 are H.

20.A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	(a) R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a}=R_{3b}=CH_3). (b) R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a}=R_{3b}=C_2H_5).
26. A chemical compound according to claim 19, wherein R_{3a} and R_{3b} are each a (C_1-C_6) alkyl group	(a) R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a}=R_{3b}=CH_3). (b) R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a}=R_{3b}=C_2H_5).
28. A pharmaceutical drug formulation comprising an effective amount of the chemical compound according to claim 1, together with a pharmaceutically acceptable excipient, diluent, or carrier.	(a) Paragraphs [0011]- [0013]; [0032]-[0064] (b) Paragraphs [0011]- [0013]; [0032]-[0064]

Thus, these two species of US'010 anticipate the subject matter recited in clams 1-3, 18-20, 26 and 28 of the '276 patent under 35 U.S.C. §102(a)(1) and §102(a)(2).

9. WO 2018/106907 (EX 1012)

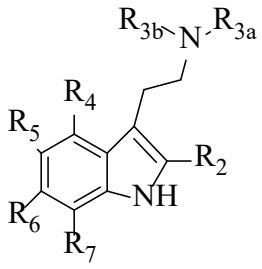
WO 2018/106907 ("WO '907") was published on June 15, 2018, which is prior to the earliest priority date of September 1, 2020, of the '276 patent. Accordingly, WO '907 is prior art to the '276 patent.

WO '907 discloses species which fall within the ambit of claims of the '276 patent. WO '907 discloses 2-(5,6-difluoro-1H-indol-3-yl)ethan-1-amine hydrochloride in Example 28 and 2-(4,6-difluoro-1H-indol-3-yl)ethan-1-amine hydrochloride in Example 61 as starting materials. WO '907 indicates that as of its filing date, both of these compounds were commercially available. The structures of these two compounds are drawn in Tables 10(a) and 10(b), respectively. The right-hand side of each of the table shows how each species described therein fall within the scope of the language of relevant claims of the '276 patent, which is described on the left-hand side of each of the tables.

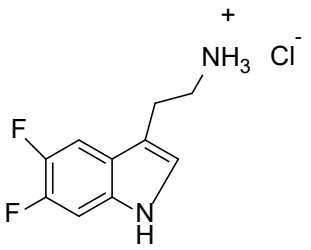
In addition, it discloses two additional species which fall within the scope of the claims of the '276 patent. Example 48 discloses 2-(4-chloro-5-fluoro-1H-indol-3-yl)ethan-1-amine

hydrochloride, while Example 49 discloses 2-(5-chloro-4-fluoro-1H-indol-3-yl)ethan-1-amine hydrochloride as starting materials. WO '907 indicates that as of its filing date, both of these compounds were commercially available. The structures of these two compounds are drawn in Tables 10(c) and 10(d), respectively. The right-hand side of each of the table shows how each species described therein fall within the scope of the language of relevant claims of the '276 patent, which is described on the left-hand side of each of the tables.

Table 10(a)



(I)

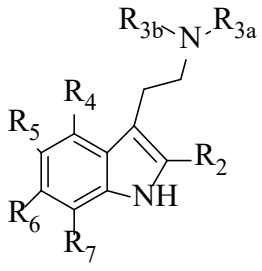


US 12,138,276	WO2018/106907 Example 28
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_5 and R_6 are both halo (R_5 and R_6 are both fluoro); R_{3a} and R_{3b} are both H, and R_2, R_4, and R_7 are all H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are R_5 and R_6 are both halo (R_5 and R_6 are both fluoro).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are R_5 and R_6 are both halo (R_5 and R_6 are both fluoro).

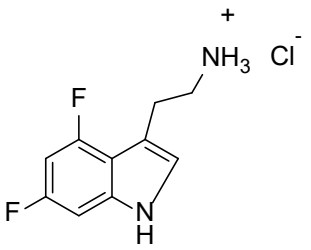
4. A chemical compound according to claim 1,wherein two of R_4, R_5, and R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are both halo (R_5 and R_6 are both fluoro).
6. A chemical compound according to claim 4, wherein R_5 is halogenated and wherein one of R_4 and R_6 is halogenated.	Salt, wherein R_5 and R_6 are both halo (R_5 and R_6 are both fluoro).
8. A chemical compound according to claim 6, wherein the halogen atoms are fluorine atoms.	Salt, wherein R_5 and R_6 are fluoro.
11. A chemical compound according to claim 8, wherein each non-halogenated R_2, R_4, R_5, R_6, or R_7, is a hydrogen atom.	Salt, wherein R_2, R_4, and R_7 are all H.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Salt, wherein R_{3a} and R_{3b} are both H.

Thus, this Example 28 invalidates claims 1-4, 6, 8, 11, and 20 of the ‘276 patent under 35 U.S.C. §102(a)(1) and 102(a)(2).

Table 10(b)



(I)

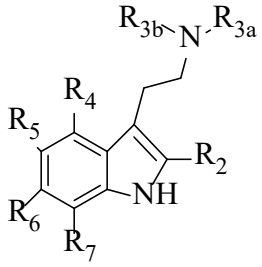


US 12,138,276	WO 2018/106907 Example 61
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a	Salt, wherein R_4 and R_6 are both halo (R_4 and R_6 are both fluoro); R_{3a} and R_{3b} are both H, and R_2, R_5, and R_7 are all H.

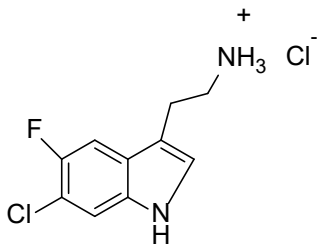
phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_4 and R_6 are both halo (R_4 and R_6 are both fluoro).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_4 and R_6 are both halo (R_4 and R_6 are both fluoro).
4. A chemical compound according to claim 1,wherein two of R_4, R_5, and R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_4 and R_6 are both halo (R_4 and R_6 are both fluoro).
5. A chemical compound according to claim 4, wherein R_4 is halogenated and wherein one of R_5 and R_6 is halogenated	Salt, wherein R_4 and R_6 are fluoro.
7. A chemical compound according to claim 5, wherein the halogen atoms are fluorine atoms.	Salt, wherein R_4 and R_6 are fluoro.
10. A chemical compound according to claim 7, wherein each non-halogenated R_2, R_4, R_5, R_6, or R_7, is a hydrogen atom.	Salt, wherein R_2, R_5, and R_7 are all H.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Salt, wherein R_{3a} and R_{3b} are both H.

Thus, the species of Example 61 of WO '907 anticipates the subject matter of claims 1-5, 7, 10, and 20 of the '276 patent under 35 U.S.C. §102(a)(1) and 102(a)(2).

Table 10(c)



(I)

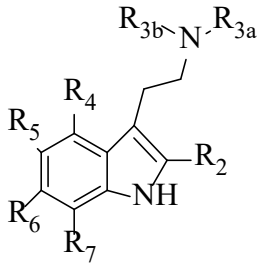


US 12,138,276	WO 2018/106907 Example 48
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_5 and R_6 are both halo (R_5 is fluoro, R_6 is chloro); R_{3a} and R_{3b} are both H, and R_2, R_4, and R_7 are all H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are halo (R_5 is fluoro, R_6 is chloro).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are halo (R_5 is fluoro, R_6 is chloro).
4. A chemical compound according to claim 1, wherein two of R_4, R_5, and R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are halo (R_5 is fluoro, R_6 is chloro).
6. A chemical compound according to claim 4, wherein R_5 is halogenated and wherein one of R_4 and R_6 is halogenated.	Salt, wherein R_5 is halo (R_5 is fluoro, R_6 is chloro).

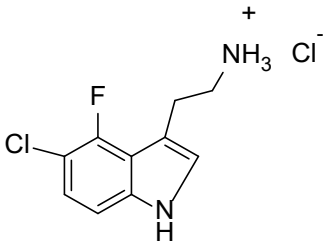
13. A chemical compound according to claim 3, wherein at least one of the halogen atoms is a chlorine atom.	Salt, wherein R_6 is chloro.
14. A chemical compound according to claim 3, wherein R_6 is a chlorine atom.	Salt, wherein R_6 is chloro.
15. A chemical compound according to claim 14, wherein R_5 is fluorine atom.	Salt, wherein R_5 is fluoro.
16. A chemical compound according to claim 14, wherein each non-halogenated R_2, R_4, R_5, R_6, or R_7, is a hydrogen atom.	Salt, wherein R_2, R_4, and R_7 are all H.
17. A chemical compound according to claim 15, wherein each non-halogenated R_2, R_4, R_5, R_6, or R_7, is a hydrogen atom	Salt, wherein R_2, R_4, and R_7 are all H.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group,	Salt, wherein R_{3a} and R_{3b} are both H.

Thus, WO '907 (Example 48) discloses a species which anticipates claims 1-4, 6, 13-17 and 20 of the '276 patent under 35 U.S.C. §102(a)(1) and 102(a)(2).

Table 10(d)



(I)



US 12,138,276	WO 2018/106907 Example 49
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_4 and R_5 are both halo (R_4 is fluoro and R_5 is chloro); R_{3a} and R_{3b} are both H: and R_2, R_6, and R_7 are all H.
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_4 and R_5 are both halo (R_4 is fluoro and R_5 is chloro).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_4 and R_5 are both halo (R_4 is fluoro and R_5 is chloro).
4. A chemical compound according to claim 1, wherein two of R_4, R_5, and R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_4 and R_5 are both halo (R_4 is fluoro and R_5 is chloro).
5. A chemical compound according to claim 4 wherein R_4 is halogenated, and wherein one of R_5 and R_6 is halogenated.	Salt, wherein R_4 and R_5 are both halo (R_4 is fluoro and R_5 is chloro).
13. A chemical compound according to claim 3, wherein at least one of the halogen atoms is a chlorine atom.	Salt, wherein R_5 is chloro.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Salt, wherein R_{3a} and R_{3b} are both H.

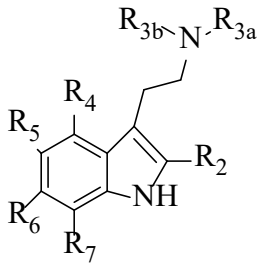
Thus, this species of WO ‘907 (Example 49) anticipates the subject matter of claims 1-5, 13 and 20 of the ‘276 patent under 35 U.S.C. §102(a)(1) and 102(a)(2).

10. Hall et al., Bioorganic & Medicinal Chemical Letters 18 (208), 2684-2690; Scheme 3, cmpd 26, p.2688 (EX 1013)

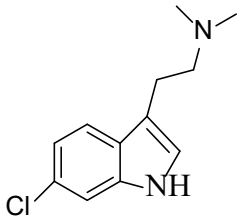
Hall et al. ("Hall et al.") published in 2008, which is prior to the earliest priority date of September 1, 2020, of the '276 patent. Accordingly, Hall et al. is prior art to the '276 patent.

Hall et al. discloses an intermediate having the formula indicated in Table 11. The right-hand side of each of the table shows how the species described therein falls within the scope of the language of relevant claims of the '276 patent, which is described on the left-hand side of the table.

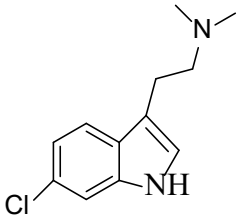
Table 11



(I)



US 12,138,276	Hall et al.
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	R_6 is halo (R_6 is (chloro); R_2, R_4, R_5, and R_7 are H; R_{3a} and R_{3b} are alkyl (R_{3a} and R_{3b} are both CH_3).
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	R_6 is halo (R_6 is (chloro).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	R_6 is halo (R_6 is (chloro).

13. A chemical compound according to claim 3, wherein at least one of the halogen atoms is a chlorine atom.	R_6 is chloro.
14. A chemical compound according to claim 3, wherein R_6 is a chlorine atom.	R_6 is chloro.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	R_{3a} and R_{3b} are both (C_1-C_6)-alkyl (R_{3a} and R_{3b} are both CH_3).
27. A chemical compound according to claim 1, wherein the chemical compound is selected from the group consisting of compounds having formulas …(XX)…. 	This is compound XX.

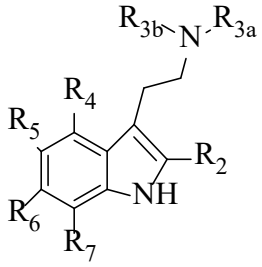
Accordingly, this compound disclosed in Hall et al. anticipates the subject matter recited in claims 1-3, 13, 14, 20, and 27 under 35 U.S.C. §102(a)(1) and 102(a)(2).

11. WO 2020/181194 (EX 1014)

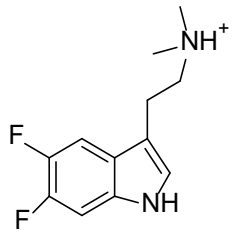
WO 2020/181194 ("WO '194") was filed internationally as a PCT application on March 6, 2020, which date is prior to the earliest priority date of September 1, 2020, of the '276 patent. Accordingly, WO '194 is prior art to the '276 patent under 35 U.S.C. §102(a)(2).

WO '194 discloses, *inter alia,* various tryptamine derivatives and analogs, such as dimethyltryptamines. It discloses, *inter alia*, mono-halo substituted tryptamines, di-halo-substituted, multi-halo-substituted tryptamines, as being 5-HT2A agonists at neuroplastogen dosages (non- psychedelic /psychotomimetic dosages), exert actions on NMDAR modulation and being useful for treating various diseases. The structures of these compounds, as drawn in WO'194, are depicted on the right-hand side in the following tables 13(a)-13(e). The right-hand side of the table shows how the species described therein fall within the scope of the language of relevant claims of the '276 patent, which is described on the left-hand side of the table.

Table 13(a)



(I)

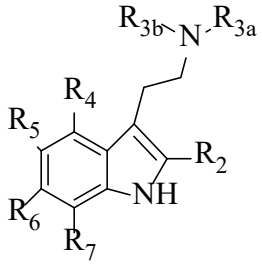


DMT 5

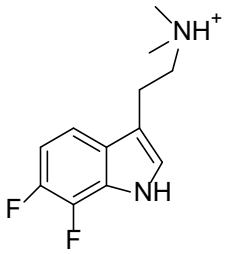
US 12,138,276	WO 2020/181194
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_5 and R_6 are halo (R_5 and R_6 are F); R_2, R_4, R_5, and R_7 are H; R_{3a} and R_{3b} are alkyl (R_{3a} and R_{3b} are CH_3).
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are halo (R_5 and R_6 are F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are halo (R_5 and R_6 are F).
4. A chemical compound according to claim 1,wherein two of R_4, R_5, and R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are halo (R_5 and R_6 are F).
6. A chemical compound according to claim 4, wherein R_5 is halogenated and wherein one of R_4 and R_6 is halogenated.	Salt, wherein R_5 and R_6 are halo (R_5 and R_6 are F).

8. A chemical compound according to claim 6, wherein the halogen atoms are fluorine atoms.	Salt, wherein R_5 and R_6 are halo (R_5 and R_6 are F).
11. A chemical compound according to claim 8, wherein each non-halogenated R_2, R_4, R_5, R_6, or R_7, is a hydrogen atom.	Salt, wherein R_2, R_4,and R_7 are each a hydrogen atom
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Salt, wherein R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} and R_{3b} are CH_3).

Table 13(b)



(I)

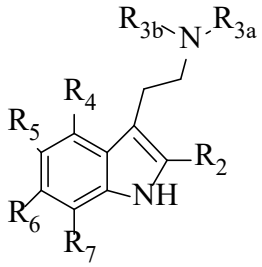


DMT 6

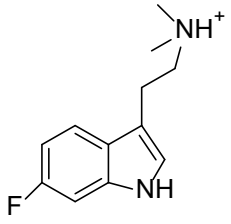
US 12,138,276	WO 2020/181194
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_6 and R_7 are halo (R_6 and R_7 are F); R_2, R_4, and R_5, are hydrogen; R_{3a} and R_{3b} are alkyl (R_{3a} and R_{3b} are CH_3).
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_6 and R_7 are halo (R_6 and R_7 are F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is	Salt wherein R_6 is halo (R_6 is F).

selected from fluorine (F), chlorine (Cl), and bromine (Br).	
20.A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Salt, wherein R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} and R_{3b} are CH_3).

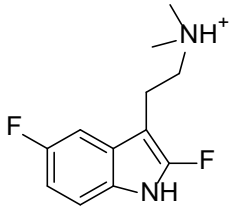
Table 13(c)



(I)



DMT 2

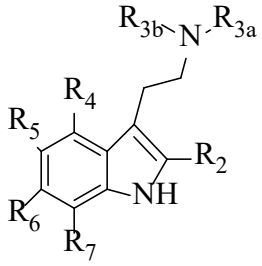


DMT 9

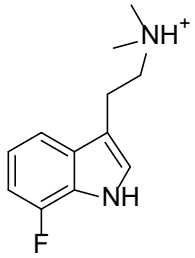
US 12,138,276	WO 2020/181194
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	DMT 2: Salt, wherein R_6 is halo (R_6 is F); R_2, R_4, R_5, and R_7 are hydrogen; R_{3a} and R_{3b} are alkyl group (R_{3a} and R_{3b} are CH_3). DMT 9: Salt, wherein R_5 and R_2 are halo (R_5 and R_2 are F); R_4, R_6, and R_7 are hydrogen; R_{3a} and R_{3b} are alkyl group (R_{3a} and R_{3b} are CH_3).
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	DMT 2: Salt wherein R_6 is halo (R_6 is F). DMT 9: Salt, wherein R_5 is halo (R_5 is F).
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	DMT 2: Salt wherein R_6 is halo (R_6 is F). DMT 9: Salt, wherein R_5 is halo (R_5 is F).
20. A chemical compound according to claim **2**, wherein R_{3a} and R_{3b} are each independently	DMT 2: Salt, wherein R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} and R_{3b} are CH_3).

selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	DMT 9: Salt, wherein R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} and R_{3b} are CH_3).

Table 13(d)



(I)

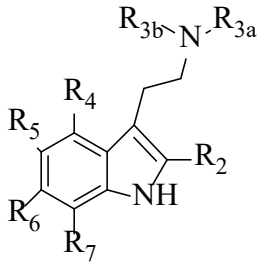


DMT 3

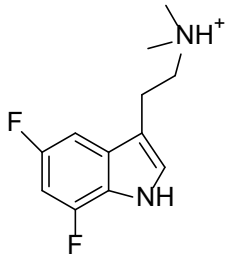
US 12,138,276	WO 2020/181194
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_7 is halo (R_7 is F); R_2, R_4, R_5, and R_6 are H; R_{3a} and R_{3b} are alkyl group (R_{3a} and R_{3b} are CH_3).
2. A chemical compound according to claim **1,** wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_7 is halo (R_7 is F).
9. A chemical compound according to claim **2,** wherein R_7 is a fluorine atom, and wherein one atom is halogenated.	Salt, wherein R_7 is halo (R_7 is F).
12. A chemical compound according to claim **9**, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7, is a hydrogen atom.	Salt, wherein R_7 is halo (R_7 is F) and R_2, R_4, R_5, and R_6 are hydrogen.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently	Salt, wherein R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} and R_{3b} are CH_3).

selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	

Table 13(e)



(I)



DMT 7

US 12,138,276	WO 2020/181194
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_5 and R_7 are halo (R_5 and R_7 are F); R_2, R_4, and R_6 are hydrogen; R_{3a} and R_{3b} are alkyl group (R_{3a} and R_{3b} are CH_3).
2. A chemical compound according to claim **1,** wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_7 are halo (R_5 and R_7 are F).
3. A chemical compound according to claim **1**, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 is halo (R_5 is F).
20. A chemical compound according to claim **2**, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Salt, wherein R_{3a} and R_{3b} are (C_1-C_6)-alkyl (R_{3a} and R_{3b} are CH_3).

Thus, the subject matter of at least claims 1-3, 4, 6, 8, 9, 11, 12, and 20 is anticipated by the teachings of WO '194 under 35 U.S.C. §102(a)(2).

12. Julia, et al., Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques (1967), 265(2), 110-112 (EX 1015)

Julia et al. ("Julia et al.") published in 1967, which date is prior to the earliest priority date of September 1, 2020, of the '276 patent. Accordingly, Julia et al. is prior art to the '276 patent under 35 U.S.C. §102(a)(1).

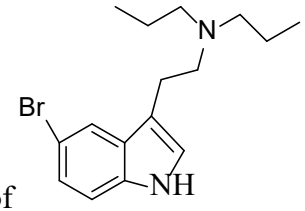
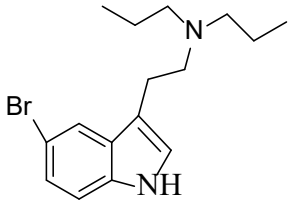
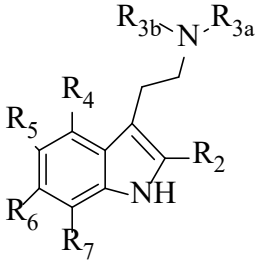
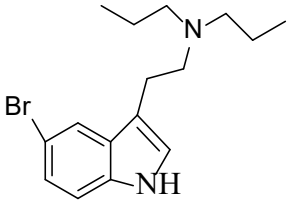
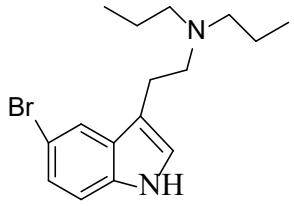
Julia et al. describe the synthesis of a salt of  . The compound  is compound XXIII of claim 27. This species is drawn on the right-hand side of the following table. The right-hand side of the table shows how the species described therein falls within the scope of the language of relevant claims of the '276 patent, which is recited on the left-hand side of the following table.

Table 14

 (I)

 ·HCl

US 12,138,276	Julia, et al.
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_5 is Br; R_2, R_3, R_4, R_6, and R_7 are H; R_{3a} and R_{3b} are both alkyl ($CH_2CH_2CH_3$)
2. A chemical compound according to claim 1 wherein one or two of R_4, R_5, R_6 or R_7 are a halogen atom, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 is Br.
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 is Br.
18. A chemical compound according to claim 3, wherein R_5 is a bromine atom, and one atom is halogenated.	Salt, wherein R_5 is Br.
19. A chemical compound according to claim 18, wherein each non-halogenated R_2, R_4, R_5, R_6 or R_7 is a hydrogen atom.	Salt, wherein R_2, R_4, R_6, R_7 are H.
20. A chemical compound according to claim 2, wherein R_{3a} and R_{3b} are each independently selected from a hydrogen atom, a (C_1-C_6)-alkyl group and a (C_1-C_6)-acyl group.	Salt, wherein R_{3a} and R_{3b} are both (C_1-C_6)-alkyl group ($CH_2CH_2CH_3$)
26. A chemical compound according to claim 19, wherein R_{3a} and R_{3b} are each a (C_1-C_6) alkyl group.	Salt, wherein R_{3a} and R_{3b} are each a (C_1-C_6) alkyl group (R_{3a} and R_{3b} are both $CH_2CH_2CH_3$).
27. A chemical compound according to claim 1, wherein the chemical compound is selected from the group consisting of compounds having formulas…() (XXII); …	This is a hydrochloride salt of compound XXIII

Accordingly, Julia et al. anticipate claims 1-3, 18, 19, 20, 26 and 27 of the '276 patent under 35 U.S.C. §102(a)(1)

13. Summary

Accordingly, claims 1-20, 24, 26-28 are anticipated by the cited prior art, and are thus invalid.

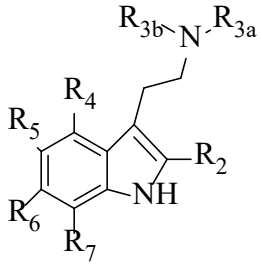
C. OBVIOUSNESS

A patent is invalid under 35 U.S.C. §103 "…if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains…" 35 U.S.C. §103. Obviousness is a legal conclusion based on the findings of at least four underlying factual factors: (1) the scope and content of the prior art; (2) the level of ordinary skill in the pertinent art; (3) the differences between the claimed invention and the claimed invention; (4) evaluation of any relevant secondary considerations. *Graham v. John Deere Co.,* 383 U.S. 1, 17-18 (1966). The Supreme Court affirmed the *Graham* analysis as the basis for determining obviousness. *KSR Int'l Co. v. Teleflex Inc.,* 550 U.S. 398, 406-407 (2007). The Federal Circuit has held that a determination for obviousness "requires not only the existence of a motivation to combine elements from different prior art references, but also that a skilled artisan would have perceived a reasonable expectation of success in making the invention via that combination." *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006).

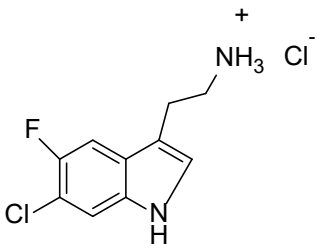
1. Claim 25 is invalid under 35 U.S.C. §103

Claim 25 of the '276 patent reads: "A chemical compound according to claim 17 wherein R_{3a} and R_{3b} are each a (C1-C6)-alkyl group." Claim 25 is ultimately dependent on several claims, as depicted in the left-hand side of the following table:

Table 15

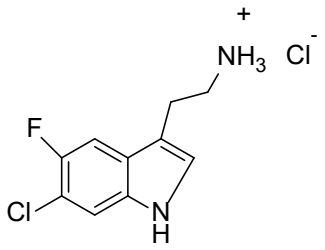


(I)



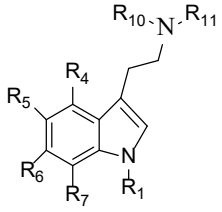
WO 2018/106907
Example 48

US 12,138,276	
1. A chemical compound or salt thereof having the formula (I): wherein at least one of R_2, R_4, R_5, R_6 or R_7 is a halogen atom, wherein each non-halogenated R_2, R_5, R_6, or R_7 is a hydrogen atom or an alkyl group or O-alkyl group, wherein R_4 when it is not halogenated is a phosphate group, a hydrogen atom or an alkyl group or O-alkyl group and wherein R_{3a} and R_{3b} are a hydrogen atom, an alkyl group, an aryl group or an acyl group.	Salt, wherein R_5 and R_6 are both halo (R_5 is fluoro, R_6 is chloro); R_{3a} and R_{3b} are both H, and R_2, R_4, and R_7 are all H.
3. A chemical compound according to claim 1, wherein one or two of R_4, R_5, or R_6 are halogenated, wherein the halogen atom is selected from fluorine (F), chlorine (Cl), and bromine (Br).	Salt, wherein R_5 and R_6 are halo (R_5 is fluoro, R_6 is chloro).
14. A chemical compound according to claim 3, wherein R_6 is a chlorine atom.	Salt, wherein R_6 is chloro.
15. A chemical compound according to claim 14, wherein R_5 is fluorine atom.	Salt, wherein R_5 is fluoro.
17. A chemical compound according to claim 15, wherein each non-halogenated R_2, R_4, R_5, R_6, or R_7, is a hydrogen atom	Salt, wherein R_2, R_4, and R_7 are all H.

The compound, 

, depicted hereinabove on the right-side of the table, is described in Example 48 of WO 2018/106907 (WO '907), which is prior art to the '276 patent. It was a commercially available starting material at the time of its filing. As shown by the above table, it falls within the scope of claims 1, 3, 14, 15, and 17. The compound differs from the subject matter of claim 25 in that R_{3a} and R_{3b} are both H, while claim 25 requires that R_{3a} and R_{3b} each be a (C_1-C_6) alkyl group.

US 2012/0029010 ("US 010") pertains to compounds of the formula



wherein, *inter alia*, R_5 and R_6 are the same or different halogens and the remaining R groups are hydroxy, oxy, halo (Br, Cl, I, Fl), C_1-C_{12}-alkoxy, C_1-C_{12}-acyloxy, amide, lower mono or dialkyl amino, aminal, thiol, C_1-C_{12}-alkylthiol, nitro, C_1-C_{12} alkysulfonyl, aminosulfonyl, hydroxyl sulfonyl, C_1-C_{12}-acylamino, sulphate, C_1-C_{12}-alkyl, C_1-C_{12}-acyl or aryl groups have, e.g., antidepressant, anxiolytic, and anti-obesity activity. US '010 teaches that the amine nitrogen can be disubstituted by alkyl groups. Thus, US '010 teaches not only that R_5 and R_6 which corresponds to R_5 and R_6 of the '276 patent, can be different halogens, but also teaches that, *inter alia*, that the amine substituents, R_{10} and R_{11}, which correspond to R_{3b} and R_{3a}, respectively of the '276 patent can be alkyl groups. It thus suggests to the skilled artisan that a N,N-dialkyl-dihalotryptamine is expected to have therapeutic properties. Thus, the combination would suggest to the skilled artisan to convert the free amine of compound of Example 48 of WO'907 to a dialkyl group.

Further, the combination of WO 2020/181194 (WO '194) with Soubhye et al. also renders obvious the subject matter of claim 25. WO '194 discloses, *inter alia*, N,N-dimethyl

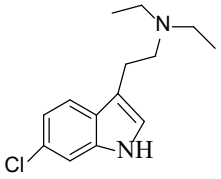
dihalo-tryptamines, such as N,N-dimethyldifluorotryptamines, are 5-HT2A agonists and that in low doses have therapeutic properties for the treatment of a multiplicity of conditions, symptoms, disorders and diseases, including but not limited to neurodegenerative diseases. One of the compounds highlighted in the table on pages 41-49 is N,N-dimethyl-5,6-difluorotryptamines.

Soubhye et al. discloses on page 8748 that 5-chlorotryptamine and 5-fluorotryptamine were both shown to be reversible inhibitors of myeloperoxidase, suggesting that chlorine can be substituted for fluorine, referring to a scientific article by Jantschko et al. in Biochemical Pharmacology, 69 (2005) 1149-1157 **(EX 1016)**. Thus, based on this teaching, the skilled artisan is motivated to replace one of the fluoro substituents on N,N-dimethyl-5,6-difluorotryptamines with chlorine, thereby producing N,N-dimethyl-5-chloro-6-fluorotryptamine, thereby producing a compound with the amino group being substituted with a dimethyl group. This falls within the ambit of claim 25 of the '276 patent, wherein the alkyl group on the amine nitrogen atom is a C_1-C_6 alkyl group.

Therefore, for the reasons provided, claim 25 is invalid under 35 U.S.C. §103.

2. Compound X in claim 27 is rendered obvious by prior art.

Compound X in claim 27 has the formula:



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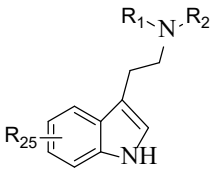
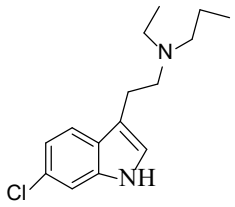
It is rendered obvious by the teachings of USSN 62/978,075 (USSN '075), which were described hereinabove. USSN '075 discloses compounds of the formula



wherein R_1 and R_2 are each selected from the group consisting of Me, Et, nPr, iPr, cyclopropyl, allyl, isobutyl and cyclopropylmethyl; and

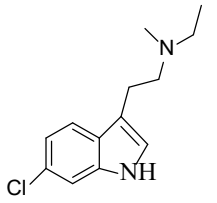
R_{25} is H, F, Cl, Br, I CF_3, Me, CN, OMe, OH, OAc, or NH_2.

USSN '075 discloses that the compounds therein are useful for treating a mood disorder and refractory depression. USSN '075 also discloses N-ethyl-N-propyl-6-chlorotryptamine having the formula:



1

and N-ethyl-N-methyl-6-chlorotryptamine having the formula:

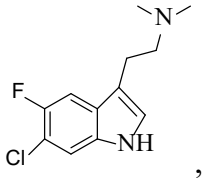


2.

Compound 1 and compound 2 differ from compound X by one CH_2 group. Compound 1 has one additional methylene group and compound 2 has 1 less methylene group. They are both homologs of compound X of claim 27. Case law has held that homologs are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563F.2d 457 (CCPA 1977). *See also In re Mayne*, 104 F.3d 1339 (Fed. Cir. 1997) (claimed protein was held to be obvious in light of structural similarities to the prior art, including known structural and functional similarity of the amino acids leucine and isoleucine.) Since compound X of the '276 patent falls within the scope of the generic formula of USSN '075, it is presumed to have the properties of the compounds of USSN '075, i.e., therapeutic properties. Accordingly, compound X of claim 27 of the '276 patent is rendered obvious.

3. Compound XXI of claim 27 is rendered obvious by prior art.

Compound XXI has the formula:

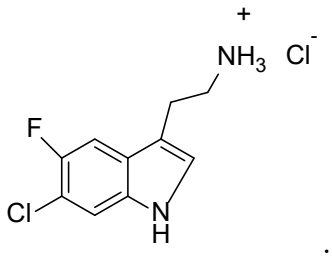


,

It is rendered obvious by the teachings of US 2012/0029010 (US '010) in view of Example 48 of WO 2018/106907 (WO '907).

The arguments presented with respect to the invalidity of claim 25 are reiterated and incorporated by reference.

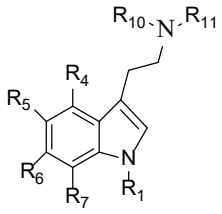
Example 48 of WO 2018/106907 (WO '907) discloses the following compound:



.

This compound differs from compound XXI of claim 27 by having an unsubstituted amino group, while compound XXI has two methyl groups substituted on the amino group.

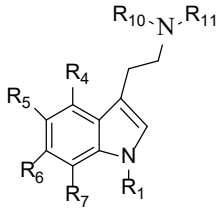
US 2012/0029010 (US '010) pertains to compounds of the formula:



wherein, *inter alia*, R_5 and R_6 are the same or different halogens and the remaining R groups are, *inter alia*, C_1-C_{12}-alkyl. It discloses that these compounds as tryptamines possess, e.g., antidepressant, anxiolytic, anti-obesity activity. US '010 teaches that the amine nitrogen can be disubstituted by alkyl groups. Thus, US '010 teaches not only that R_5 and R_6, which corresponds to R_5 and R_6 of the '276 patent, can be the same or different halogens. It also teaches that, *inter alia*, that the amine substituents, R_{10} and R_{11}, which correspond to R_{3b} and R_{3a}, respectively of the '276 patent can be alkyl groups. It further discloses compounds, such as N,N-dimethyl-5-

bromotryptamine as being useful for treating depression and anxiety, i.e., having therapeutic properties.

For the reasons provided above, the skilled artisan would be motivated to combine the compound of WO'907 with N,N-dimethyl-5, 6-difluorotryptamine of US '010 to obtain a compound of the formula



,

wherein R_5 is fluoro, R_6 is chloro, R_{10} and R_{11} each being methyl and R_1, R_4, and R_7 being hydrogen, and expect that such compound would have therapeutic properties. Thus, the combination of US'010 in view of Example 48 of WO '907 would have suggested and motivated the skilled artisan to prepare compound XXI.

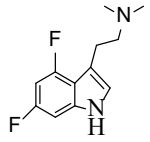
Further, the combination of WO 2020/181194 (WO '194) with Soubhye et al., also renders obvious compound XXI. WO '194 discloses, *inter alia*, that N,N-dimethyl-dihalo-tryptamines, such as N,N-dimethyldifluorotryptamines are 5-HT2A agonists and in low doses have therapeutic properties, as described hereinabove.

Soubhye et al. disclose on page 8748 that 5-chlorotryptamine and 5-fluorotryptamine were both shown to be efficient reversible inhibitors of myeloperoxidase, suggesting that chlorine can be substituted for fluorine. Thus, based on this teaching, the skilled artisan is motivated to replace one of the fluoro substituents on N,N-dimethyl-5,6-difluorotryptamines with chlorine, thereby producing N,N-dimethyl-5-chloro-6-fluorotryptamine, which is compound XXI.

Therefore, for the reasons provided, compound XXI is obvious.

4. Compound XXIII of claim 27 is rendered obvious by prior art.

Compound XXIII of claim 27 of the '276 patent has the formula:



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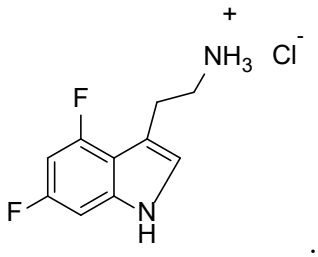
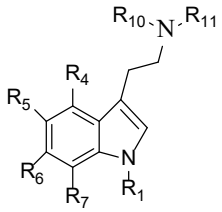
WO 2018/106907 (WO '907) in Example 61 discloses the following compound:



.

This compound differs from compound XXIII of claim 27 of the '276 patent by having an unsubstituted amino group, while compound XXIII has two methyl groups substituted on the amino group.

US 2012/0029010 (US '010) pertains to compounds of the formula

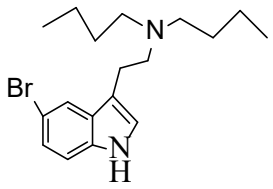


wherein, *inter alia*, R_5 and R_6 are the same or different halogens and the remaining R groups are, *inter alia*, C_1-C_{12}-alkyl. It discloses that the tryptamines have various pharmaceutical utilities. US '010 teaches that the amine nitrogen can be disubstituted by alkyl groups. Thus, US '010 teaches not only that R_5 and R_6 which corresponds to R_5 and R_6 of the '276 patent, can be the same or different halogens. It also teaches that, *inter alia*, that the amine substituents, R_{10} and R_{11}, which correspond to R_{3b} and R_{3a}, respectively of the '276 patent can be alkyl groups. It further teaches that N,N-dialkyl-dihalotryptamines would have therapeutic properties

Thus, the combination of US '010 and Example 61 of WO '907 would have suggested and motivated the skilled artisan to obtain Compound XXIII and Compound XXIII is rendered obvious.

5. Compound XXIV of claim 27 is rendered obvious by prior art.

Compound XXIV of claim 27 having the formula:



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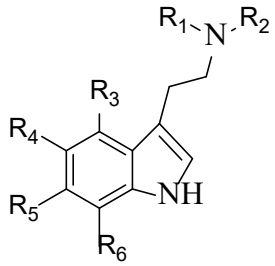
is rendered obvious by the teachings in USSN '075 in view of Julia, et al.

USSN '075 describes, *inter alia*, a tryptamine compound useful for treating mood disorders of the formula:



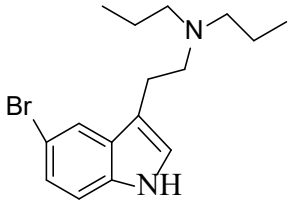
wherein

R_1, R_2 = Me, Et, nPr, iPr, cyclopropyl, allyl, isobutyl, cyclopropylmethyl;

R_3-R_7=H, F, Cl, Br, I, CF_3, Me.

This compound encompasses compounds wherein R_4 is bromo, R_3, R_5 and R_6 are hydrogen, and R_1 and R_2 are both n-propyl or isobutyl.

Julia et al. discloses the compound



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When the compound of USSN '075 is defined as R_4 is bromo, R_3, R_5 and R_6 are hydrogen, and R_1 and R_2 are both n-propyl , it is a homolog of Compound XXIV. *See, In re Wilder*, 563 F.2d 457 (CCPA 1977) and *In re Mayne*, 104 F.3d 1339 (Fed. Cir. 1997) described *supra*. Accordingly, the skilled artisan would be motivated to prepare the homolog of the compound in Julia et al. that is, the dibutylamine analog of the compound disclosed in Julia et

al. Based on the similarity of structures between the compound in Julia et al. and compound XXIV of claim 27 of the '276 patent, there is a presumption that compound XXIV of claim 27 of the '276 patent is also useful for treating mood disorders and refractory depression. Moreover, since compound XXIV of the '276 patent falls within the scope of the generic formula of US '048 and since the tryptamine compound in Julia et al. has identical alkyl groups on the amino nitrogen atom, the skilled artisan would be motivated to prepare the next homolog in the series having the amino nitrogen being substituted with two n-butyl substituents. Accordingly, for these reasons, compound XXIV of claim 27 of the '276 patent is rendered obvious.

6. Claim 29 is invalid under 35 U.S.C. §103.

For the reasons presented hereinabove, prior art teaches or suggests that compounds X, XX, XXII, XXIII, XXIV of claim 27 have therapeutic utility.

US 2012/0029010 (US '010) discloses drug formulation comprising an active compound with a pharmaceutical carrier, diluent, and/or excipient. Consequently, with respect to each species described in the previous sections, it would be obvious to combine the compounds described hereinabove in each of the sections with a pharmaceutically acceptable excipient, diluent, or carrier in a pharmaceutical composition. Such combination would render obvious the subject matter of claim 29 of the '276 patent.

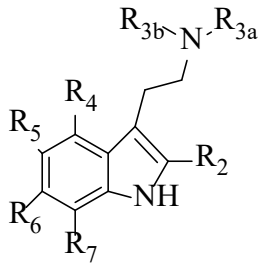
VI. CLAIM 1 IS NOT ENABLED AND IS INDEFINITE

35 U.S.C. §112(a) reads:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

Case law has held that the breadth of enablement must be commensurate in scope with the claims. *See*, *Enzo Biochem, Inc. v. Calgene, Inc*., 188 F.3d 1362 (Fed. Cir. 1999).

Claim 1 is directed to a compound of formula I below



wherein the variables are defined as described herein. This is a broad scope, as the exemplification does not show how to prepare compounds wherein three or more of R_2, R_3, R_4, R_5, R_6, and R_7 are other than hydrogen or halogen. The '276 patent provides two methods of preparing the compounds therein. One is using a biosynthetic system which utilizes cells comprising a psilocybin biosynthetic enzyme complement. Preparing the compounds by this method requires the selection of a psilocybin precursor compound; although the specification provides examples thereof, it does not provide any guidance as to how to select the appropriate precursor to prepare a desired compound other than what is exemplified. None of the exemplified compounds have more than two of R_2, R_3, R_4, R_5, R_6, and R_7 being substituted. Moreover, the specification does not provide any guidance as to which psilocybin biosynthetic enzyme complement to use to prepare a desired compound, other than what is exemplified. The second method is a synthetic method, but there is no exemplified chemistry illustrating how to prepare compounds wherein one of R_2, R_3, R_4, R_5, R_6, and R_7 is halogen and at least two are O-alkyl or R_4 is phosphate or O-alkyl, one of R_2, R_3, R_5, R_6, and R_7 is halogen, and at one of the remaining variables is O-alkyl. The amount of direction presented, and the number of working examples provided in the specification are very narrow compared to the wide breadth of the claims at issue. Moreover, chemistry is an unpredictable art. *In re Fisher*, 166 USPQ 18, 25 (CCPA 1970). The amount of experimentation required to prepare these type of compounds is quite high. Thus, considering the Wands factors, there is an undue amount of experimentation required and the claim is invalid as lacking enabling support. Moreover, for the reasons enumerated in section IV. *supra*, claim 1 is indefinite under 35 U.S.C. §112(b) and thus invalid.

VII. DISCRETIONARY DENIAL IS NOT APPROPRIATE UNDER § 325(d)

The Board should not exercise its discretion under § 325(d) to deny institution. The Board has outlined factors it considers in determining whether to exercise discretion to deny institution under § 325(d). *See Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8, 17-18 (Dec. 15, 2017) (precedential as to § III.C.5, first paragraph); *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6, 8-11 (Feb. 13, 2020) (precedential). *Advanced Bionics* explains how the *Becton, Dickinson* factors fit into a two-part framework that examines:

> (1) whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office; and
>
> (2) if either condition of first part of the framework is satisfied, whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.

Advanced Bionics at 8. In evaluating this first factor, the Board looks to *Becton, Dickinson* factors (a), (b), and (d). *Id*. at 9-10. Factor (a) under the *Becton, Dickinson* construct assesses "the similarities and material differences between the asserted art and the prior art involved during examination." *Id*. at 9 n.10. Factor (b) considers "the cumulative nature of the asserted art and the prior art evaluated during examination." *Id*. Factor (d) weighs "the extent of the overlap between the arguments made during examination and the manner in which petitioner relies on the prior art." *Id*.

"If, after review of factors (a), (b), and (d), it is determined that the same or substantially the same art or arguments previously were presented to the Office, then factors (c), (e), and (f) relate to whether the petitioner has demonstrated a material error by the Office." *Id*. at 10. Factor (c) assesses "the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection." *Id*. at 9 n.10. Factor (e) analyzes "whether petitioner has pointed out sufficiently how the examiner erred in its evaluation of the asserted prior art." *Id*. Factor (f) considers "the extent to which additional evidence and facts presented in the petition warrant reconsideration of the prior art or arguments." *Id*.

Advanced Bionics counsels against the Board exercising discretionary denial here.

Notably, the prosecution history does not reflect that the Examiner ever appreciated or considered the prior art identified and described herein. Except for the restriction requirement, the prosecution history of the '276 patent reflects that the Examiner did not apply any art during the prosecution of the underlying application. In addition, the art described hereinabove was not cited either by the patentee or the Examiner. The art cited herein is new art never considered by the Examiner. Moreover, the Board would serve the public by providing a forum to invalidate claims in a patent that contains so many claims that are at least anticipated by multiple prior art references. Accordingly, based on the new art cited herein, the additional evidence and facts presented in this Petition, it is respectfully submitted that this Petition warrants reconsideration of the patentability of claims 1-20 and 24-29.

VIII. MANDATORY NOTICES

A. REAL PARTY-IN-INTEREST UNDER 37 C.F.R. § 42.8(B)(1)

The real party-in-interest is Gilgamesh Pharmaceuticals, Inc., located at 113 University Place, Suite 1019, New York, New York 10003. No unnamed entity is funding, controlling, or otherwise has an opportunity to control or direct this Petition or Petitioner's participation in any resulting PGR.

B. RELATED MATTERS UNDER 37 C.F.R. § 42.8(B)(2)

Petitioner is not aware of any related matters that would affect or be affected by this proceeding.

C. LEAD AND BACK-UP COUNSEL UNDER 37 C.F.R. § 42.8(B)(3)

Petitioner designates lead and back-up counsel as noted below. Powers of attorney pursuant to 37 C.F.R. §42.10(b) accompany this Petition.

Lead Counsel	Back-Up Counsel
Peter I. Bernstein (Reg. No. 43,497) pibernstein@ssmp.com SCULLY SCOTT MURPHY & PRESSER PC 400 Garden City Plaza Suite 300 Garden City, N.Y. 11530 Tel: 516 742-4343	Mark J. Cohen (Reg. No. 32,211) markjcohen@ssmp.com SCULLY SCOTT MURPHY & PRESSER PC 400 Garden City Plaza Suite 300 Garden City, N.Y. 11530 Tel: 516 742-4343

Fax: 516 742-4366	Fax: 516 742-4366

D. Service Information Under 37 C.F.R. § 42.8(b)(4)

Please address all correspondence to the lead and back-up counsel at the addresses shown above. Petitioner consents to service by email at the addresses of lead and back-up counsel shown above, as well as intprop@ssmp.com.

IX. GROUNDS FOR STANDING

Pursuant to 37 C.F.R. § 42.204(a), Petitioner certifies that the '276 patent is available for PGR and that (1) neither Petitioner nor any of its privies own the '276 patent; and (2) neither Petitioner nor any of its privies have filed a U.S. civil action challenging the validity of any claim of the '276 patent. This Petition was filed within nine months of the '276 patent issuing. The '276 patent is subject to the Leahy-Smith America Invents Act ("AIA") and thus eligible for PGR because at least one claim in a patent to which the '276 patent claims priority has an effective filing date after the effective date of the AIA.

X. CONCLUSION

The challenged claims should be canceled for the reasons discussed above.

Respectfully submitted,

August 12, 2025

By: /Peter I. Bernstein/
Peter I. Bernstein (43,497)
Mark J. Cohen (32,211)
SCULLY SCOTT MURPHY & PRESSER, P.C.

Counsel for Petitioner Gilgamesh Pharmaceuticals, Inc.

CERTIFICATION UNDER 37 C.F.R. § 42.24(d)

Pursuant to 37 C.F.R. § 42.24(a)(1)(ii), the undersigned hereby certifies that the foregoing PETITION FOR POST GRANT REVIEW contains 18,570 words, excluding the parts of this petition that are exempted under 37 C.F.R. § 42.24(a), as measured by the word-processing system used to prepare this paper.

By: /Peter I. Bernstein/
Peter I. Bernstein (43,497)
Mark J. Cohn (32,211)
SCULLY SCOTT MURPHY & PRESSER, P.C.

Counsel for Petitioner Gilgamesh Pharmaceuticals, Inc.

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§ 42.6(e) and 42.205(a), the undersigned certifies that on August 12, 2025, a copy of the foregoing **Petition for Post-Grant Review, the associated power of attorney**, and **Exhibits 1001-1016** were served by Priority Mail Express (ER 210 393 228 US) on the correspondence address of record indicated in the Patent Office's Patent Center website for U.S. Patent No. 12,138,276:

Smart & Biggar LP
40 King Street West, 40th Floor,
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Dated: August 12, 2025

By: /Peter I. Bernstein/
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Counsel for Petitioner Gilgamesh Pharmaceuticals, Inc.