

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PADAGIS US LLC,

Petitioner

v.

NEURELIS, INC.,

Patent Owner.

Case No. IPR2025-00466
U.S. Patent No. 11,793,786

PATENT OWNER'S RESPONSE

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2074	Declaration of Dr. Marc Brown regarding U.S. Patent No. 11,793,786
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TABLE OF CHALLENGED CLAIMS

Claim Element	Claim Language from '786 Patent
1(Preamble)	1. A pharmaceutical solution for nasal administration consisting of:
1(a)	a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof;
1(b)	one or more natural or synthetic tocopherols or tocotrienols selected from the group consisting of α -tocopherol, β -tocopherol, γ -tocopherol, δ -tocopherol, α -tocotrienol, β -tocotrienol, γ -tocotrienol, δ -tocotrienol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w);
1(c)	one or more alcohols in an amount from 10% to 70% (w/w), wherein the one or more alcohols comprises benzyl alcohol; and
1(d)	n-dodecyl beta-D-maltoside.
2	2. The pharmaceutical solution of claim 1, wherein the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof is present in the pharmaceutical solution in a concentration from 1 to 20% (w/v).
3	3. The pharmaceutical solution of claim 1, wherein the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof is present in the pharmaceutical solution in a concentration from 10 mg/mL to 250 mg/mL.
4	4. The pharmaceutical solution of claim 3, wherein the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof is present in the pharmaceutical solution in a concentration from 20 mg/mL to 50 mg/mL.
5	5. The pharmaceutical solution of claim 1, wherein the one or more natural or synthetic tocopherols or tocotrienols is in an amount from 45% to 85% (w/w).
6	6. The pharmaceutical solution of claim 5, wherein the one or more natural or synthetic tocopherols or tocotrienols is in an amount from 60% to 75% (w/w).
7	7. The pharmaceutical solution of claim 1, wherein the one or more alcohols is benzyl alcohol and a second alcohol selected from ethanol, propyl alcohol, butyl alcohol, pentanol, any isomers thereof, and any combinations thereof.

Claim Element	Claim Language from '786 Patent
8	8. The pharmaceutical solution of claim 1, wherein the one or more alcohols are in an amount from 15% to 55% (w/w).
9	9. The pharmaceutical solution of claim 8, wherein the one or more alcohols are in an amount from 25% to 40% (w/w).
10	10. The pharmaceutical solution of claim 1, wherein the solution consists of diazepam, vitamin E, benzyl alcohol, and n-dodecyl beta-D-maltoside.
11(preamble)	11. A pharmaceutical solution for nasal administration consisting of:
11(a)	a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof;
11(b)	one or more natural or synthetic α -tocopherols selected from the group consisting of tocopherol, β -tocopherol, γ -tocopherol, δ -tocopherol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w);
11(c)	one of more alcohols in an amount from 10% to 70% (w/w)), wherein the one or more alcohols comprises benzyl alcohol;
11(d)	and n-dodecyl beta-D-maltoside.
12	12. The pharmaceutical solution of claim 11, wherein the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof is present in the pharmaceutical solution in a concentration from 1 to 20% (w/v).
13	13. The pharmaceutical solution of claim 11, wherein the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof is present in the pharmaceutical solution in a concentration from 10 mg/mL to 250 mg/mL.
14	14. The pharmaceutical solution of claim 13, wherein the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof is present in the pharmaceutical solution in a concentration from 20 mg/mL to 50 mg/mL.
15	15. The pharmaceutical solution of claim 11, wherein the one or more natural or synthetic tocopherols is in an amount from 45% to 85% (w/w).
16	16. The pharmaceutical solution of claim 15, wherein the one or more natural or synthetic tocopherols is in an amount from 60% to 75% (w/w).

Claim Element	Claim Language from '786 Patent
17	17. The pharmaceutical solution of claim 11, wherein the one or more alcohols is benzyl alcohol and a second alcohol selected from ethanol, propyl alcohol, butyl alcohol, pentanol, any isomers thereof, and any combinations thereof.
18	18. The pharmaceutical solution of claim 11, wherein the one or more alcohols are in an amount from 15% to 55% (w/w).
19	19. The pharmaceutical solution of claim 18, wherein the one or more alcohols are in an amount from 25% to 40% (w/w).
20	20. The pharmaceutical solution of claim 1, wherein the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof present in the pharmaceutical solution is from about 5 to about 20 mg.
21	21. The pharmaceutical solution of claim 11, wherein the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof present in the pharmaceutical solution is from about 1 mg to about 20 mg.
22	22. The pharmaceutical solution of claim 1, wherein the n-dodecyl beta-D-maltoside is present in the pharmaceutical solution in an amount from about 0.01% (w/v) to about 1% (w/v).
23	23. The pharmaceutical solution of claim 11, wherein the n-dodecyl beta-D-maltoside is present in the pharmaceutical solution in an amount from about 0.01% (w/v) to about 1% (w/v).
24	24. The pharmaceutical solution of claim 1, wherein the n-dodecyl beta-D-maltoside is present in the pharmaceutical solution in an amount from about 0.125% (w/v) to about 0.5% (w/v).
25	25. The pharmaceutical solution of claim 11, wherein the n-dodecyl beta-D-maltoside is present in the pharmaceutical solution in an amount from about 0.125% (w/v) to about 0.5% (w/v).
26	26. The pharmaceutical solution of claim 1, wherein the α -tocopherol is Vitamin E USP.
27	27. The pharmaceutical solution of claim 11, wherein the α -tocopherol is Vitamin E USP.

I. INTRODUCTION

Neurelis, Inc. (“Neurelis” or “Patent Owner”) submits this Patent Owner Response to the Petition for IPR (“Petition” or “Pet.”) filed by Padagis (“Petitioner”), challenging claims 1-27 of U.S. Patent No. 11,793,786 (“’786 Patent”) (EX1001) as obvious. This Response is supported by the declarations of Dr. Marc Brown (EX2074) and three of the ’786 Patent inventors: Cartt, Mitchnick, and Maggio (EX2045-EX2047).

“The inventor’s own path itself never leads to a conclusion of obviousness; that is hindsight.” *Otsuka Pharm. Co., Ltd. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012). Petitioner’s choice to follow this path pervades its Petition.

First, Gwozdz-PCT (EX1009),¹ the principal reference, is not prior art under 35 U.S.C. §102(e) (pre-AIA) because the ’786 Patent is entitled to a priority date that eliminates this reference. Gwozdz-PCT purports to trace priority to March 28, 2008 (61/040,281), but the ’786 Patent also traces priority to March 28, 2008 (61/040,558). The two provisional applications were filed the same day by a joint research group because they disclosed different inventions, which is why Petitioner

¹ To distinguish the reference from the inventor, EX1009 is referred to as “Gwozdz-PCT.”

does not assert any anticipation grounds. Gwozdz-PCT is not “by another ... before the invention” of the ’786 Patent, so Gwozdz-PCT does not qualify as prior art.

This circumstance is no accident. The ’786 Patent inventors, which included inventors from both Gwozdz-PCT and Meezan (highlighted below), filed two provisionals the same day—the ’558 Provisional application (leading to the ’786 Patent) and the ’281 Provisional (leading to Gwozdz-PCT)—to obviate the invalidity challenge that Petitioner makes in these proceedings.

'786 Patent (EX1001)	Inventors: Steve Cartt , Hillsborough, CA (US); David Medeiros , Sparks, NV (US); Garry Thomas Gwozdz , Jim Thorpe, PA (US); Andrew Loxley , Brussels (BE); Mark Mitchnick , East Hampton, NY (US); David F. Hale , San Diego, CA (US); Edward T. Maggio , San Diego, CA (US)
WO2009/120933 Gwozdz-PCT (EX1009)	Inventors; and Inventors/Applicants <i>(for US only)</i> : GWOZDZ, Garry, Thomas [US/US]; 329 South Main Street, Nazareth, PA 18064 (US). LOXLEY, Andrew [GB/US]; 126 Market Street, #5, Philadelphia, PA 19106 (US). MITCHNICK, Mark [US/US]; 80 Three Mile Harbor Drive, East Hampton, NY 11937 (US).
US2006/0046962 Meezan (EX1010)	Inventors: Elias Meezan , Birmingham, AL (US); Dennis J. Pillion , Hoover, AL (US); Edward T. Maggio , San Diego, CA (US)

In Ground 2, Petitioner relies on another reference developed by the ’786 inventors:

US2008/0279784 Cartt-784 (EX1065)	Inventors: Steve Cartt, Union City, CA (US); David Medeiros, South San Francisco, CA (US)
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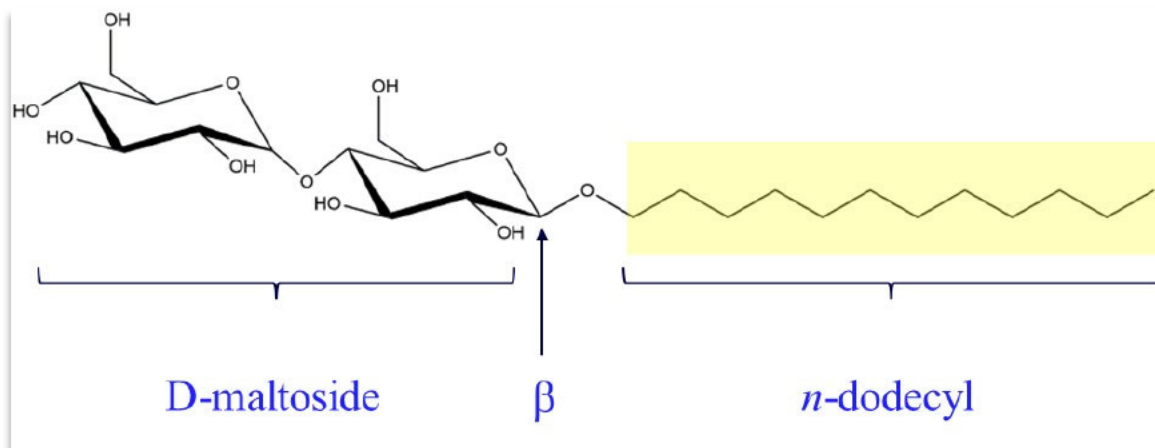
Nevertheless, Petitioner asks the Board to reject Neurelis’s right to priority, and then modify Gwozdz-PCT with Meezan to reconstruct the challenged claims by re-tracing the steps of the ’786 Patent inventors. This tactic is improper. “What matters is the path that the person of ordinary skill in the art would have followed, as evidenced by the pertinent prior art,” not the path the inventors forged. *Millenium Pharms., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367 (Fed. Cir. 2017) (quoting *Otsuka*, 678 F.3d at 1296).

Second, regardless of whether Gwozdz-PCT qualifies as §102(e) prior art, it is unavailable for obviousness under 35 U.S.C. §103(c) (as is Cartt-784), as they were developed under a joint research agreement. Once again, Petitioner’s choice to draft off the inventors’ work is precluded.

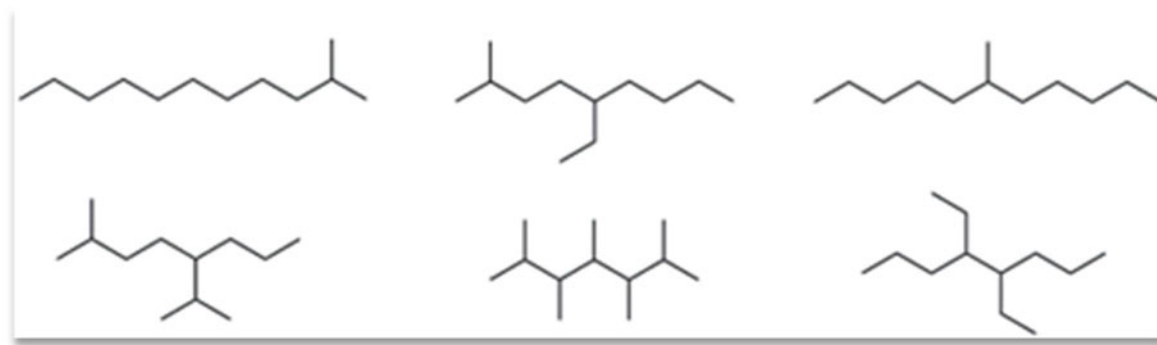
Third, the putative prior art here provides no tracks that a POSA would have followed to the claimed inventions: (a) the references fail to disclose all claim limitations; and (b) there would have been no motivation to combine, absent Petitioner’s hindsight perspective on the inventors’ own work.

Petitioner failed to establish that all claim limitations are disclosed or taught by the combinations. This infirmity alone suffices to reject Petitioner’s obviousness

assertions. *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014). Every challenged claim recites “*n*-dodecyl beta-D-maltoside” (depicted below), which is a specific chemical compound having a 12-carbon chain (“dodecyl”) in a linear (“*n*”) configuration, as opposed to a branched configuration.



While Meezan discloses *other* alkyl glycosides, the specific compound claimed in the '786 Patent *is not disclosed*. Of particular significance, Meezan does not disclose or suggest a *linear* dodecyl chain; instead it discloses using “highly branched” chains. EX1010 ¶[0149]. Even considering just the “dodecyl” piece (highlighted above), there are 354 other isomers of dodecyl disclosed in Meezan, all of which are branched and none of which is linear. Exemplary branched dodecyl isomers are shown below.



EX2074 ¶¶72, 81.

There is a gaping hole in the Petition and Dr. Donovan’s declaration, as they do not identify any disclosure or teachings of the “*n*-” (linear) dodecyl moiety. At deposition, Dr. Donovan did not even know to what structural configuration “*n*-” refers. EX2070, 193:2-25. Thus, Petitioner overlooked that the only structural configuration for alkyl glycosides disclosed in the obviousness combination is “branched,” not the claimed linear or “*n*-.” See *Univ. of Strathclyde v. Clear-Vu Lighting LLC*, 17 F.4th 155, 160-161 (Fed. Cir. 2021) (overturning “the Board’s erroneous finding that the prior art disclosed all claim limitations”). Petitioner and Dr. Donovan have no explanation for this missing claim limitation. The ’786 Patent claims must be upheld. See 37 C.F.R. §42.104(b)(4) (“petition must specify where each element of the claim is found in the prior art”); 35 U.S.C. §312(a)(3)-(a)(4) (similar).

A POSA viewing Meezan at the priority date, rather than with hindsight, would have understood it to disclose legions of alkyl glycosides of varying alkyl-

chain lengths. For a POSA to have chosen *any* form of dodecyl (12-carbon) maltoside—absent hindsight—would have required an incredible stroke of fortune. *See In re Kuban*, 561 F.3d 1351, 1359 (Fed. Cir. 2009) (“where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness”).

Moreover, Gwozdz-PCT discloses a complete solution for the problem it addressed. Rather than supply any motivation to combine, Petitioner uses the '786 Patent itself to identify the problem, solves that problem with Gwozdz-PCT, and adds Meezan solely because the '786 claims require an additional ingredient that Meezan purportedly discloses (but does not). Such hindsight cannot serve as a basis for invalidity.

Lastly, as an end-around the substantive deficiencies with its invalidity argument, Petitioner contends that Neurelis should be unable to defend the '786 Patent on account of collateral estoppel. But the '786 Patent was not the subject of any prior judicial proceeding. The only prior proceeding, IPR2019-00451 (“451 IPR”), concerned Patent No. 9,763,876 (“’876 Patent”). This is a different patent from a separate branch of the family tree with different patent claims, different claims of priority, and different issues of patentability.

II. THE '786 PATENT AND THE CHALLENGED CLAIMS

A. PROSECUTION HISTORY

The '786 Patent issued from Application 17/228,514 that ultimately claims priority to the '558 Provisional (filed March 28, 2008). When filing the '514 Application, Neurelis submitted the art on which this Petition relies, including the record from the 451 IPR. EX1002 at 374-394, 487-515.

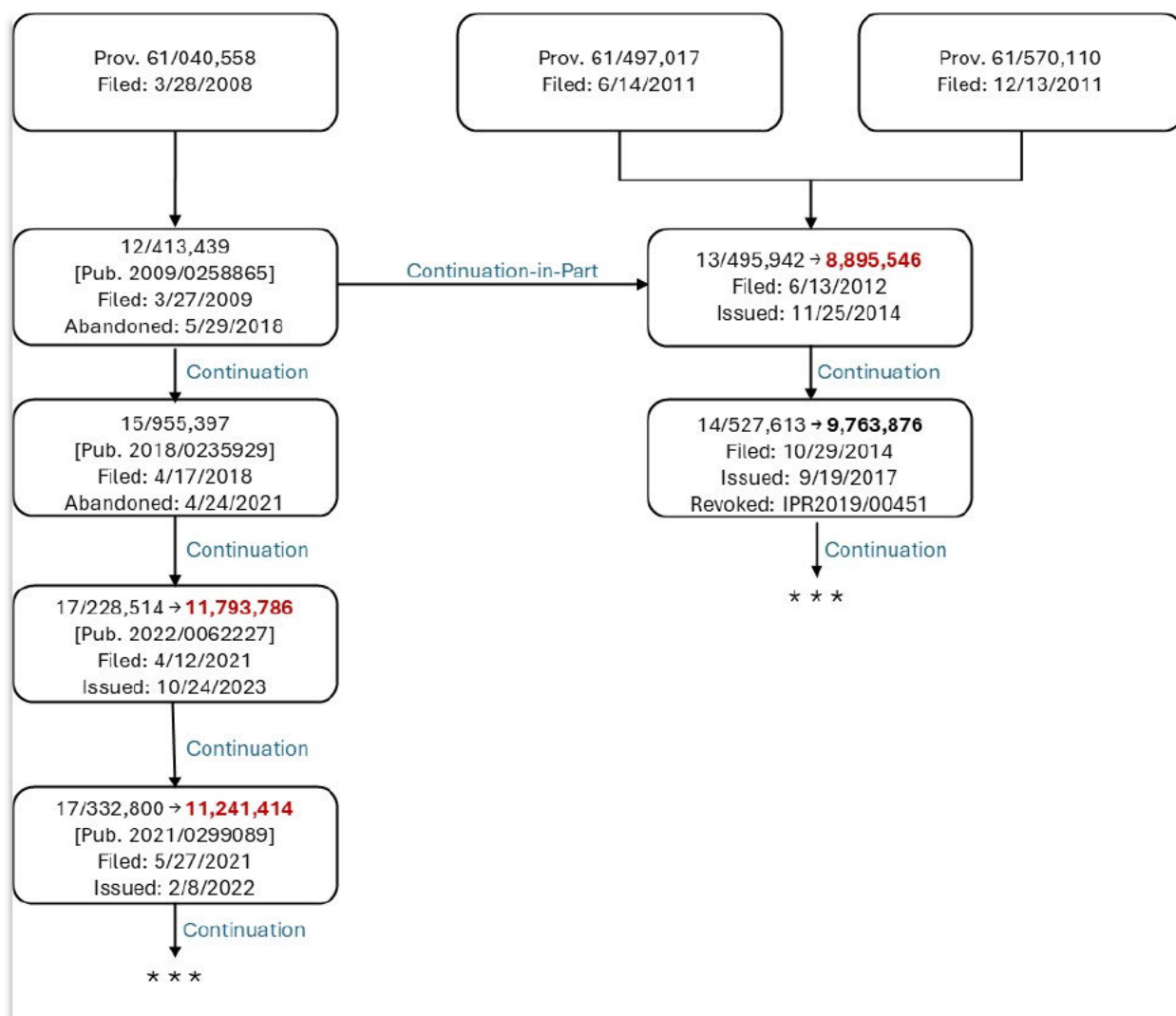
B. THE CLAIMED INVENTION

The '786 Patent provides a pharmaceutical solution containing both tocopherols or tocotrienols (e.g., vitamin E) and alcohols (e.g., ethanol and benzyl alcohol), which readily dissolve diazepam while maintaining appropriate viscosity. EX1001, 35:27-37.

The '786 Patent claims Valtoco®, a pharmaceutical solution of diazepam that an acquaintance or family member of a patient can administer to treat acute bouts of seizure clusters. EX1001 at 18:64-19:3. Valtoco® was approved in January 2020 and awarded Orphan Drug Exclusivity because it possesses clinical superiority and provides “a major contribution to patient care.” 21 C.F.R. §316.3(b)(3)(iii); EX2001 at 4; EX2074 ¶¶114-117.

C. FAMILY TREE

A summary of relevant patents and applications is shown below, with those challenged by Padagis in red.



EX2068.

III. LEVEL OF ORDINARY SKILL

A person of ordinary skill in the art (“POSA”) has the following qualifications:

[T]he skilled artisan holds a Master’s degree with many years of experience, or a Ph.D. or Pharm.D degree with several years of experience or its equivalent experience in the field of pharmaceutical research and development. The skilled artisan would have knowledge of benzodiazepine structure and function, including physiochemical

characteristics of benzodiazepines generally. The skilled artisan would further have knowledge and practical experience developing and working with intranasal formulations, including knowledge of the physiology and anatomy of the nasal cavity and methods of administering drugs intranasally. The skilled artisan also would have knowledge concerning clinical aspects of bioavailability, tolerability, and patient acceptability of intranasal formulations and the difficulty of administering drugs by other routes during an event like a seizure.

EX2074 ¶¶61-62.

IV. CLAIM CONSTRUCTION

“[W]hen a petitioner takes alternative [claim construction] positions before the Board and a district court, that petitioner should, at a minimum, explain why alternative positions are warranted.” *Revvo Techs., Inc. v. Cerebrum Sensor Techs., Inc.*, IPR2025-00632, Paper 20 at 3-4 (P.T.A.B. Nov. 3, 2025) (precedential). Gamesmanship “does not further the Office’s goal of ‘providing greater predictability and certainty in the patent system.’” *Id.* at 4. Here, Petitioner’s obviousness challenge requires applying a construction of the “consisting of” language that directly contradicts Petitioner’s construction in district court. Petitioner contends there that the claims preclude even trace amounts of water, yet here relies on aqueous embodiments of both Gwozdz-PCT and Meezan to argue obviousness.

A. PETITIONER’S DISTRICT COURT POSITION FOR “CONSISTING OF”

Independent claims 1 and 11 recite, “A pharmaceutical solution for nasal administration consisting of” several ingredients. In district court, the parties dispute what “consisting of” means:

Term	Neurelis’s Position	Padagis’s Construction
A pharmaceutical solution for nasal administration consisting of	No construction necessary; the scope of “consisting of” is established by law.	“a pharmaceutical solution for nasal administration containing only those elements set forth in the claim and excluding anything else, particularly excluding water and oil” Otherwise indefinite.

EX2050 (Joint-CC Br.) at 27. Although Petitioner *now* contends in IPR that “consisting of” needs no construction, Petitioner in district court asserts that it means “excluding anything else, particularly excluding water and oil”; the claims cannot include even “trace impurities” of water or oil. *Id.* at 27, 46. If the claims are construed to allow any amount of water or oil, Petitioner contends the claims are indefinite because a POSA could not reasonably ascertain their scope. *Id.* at 53-57.

In support of its construction, Petitioner provided a declaration from Dr. Donovan—the same expert supporting its petition—stating that “the ‘consisting of’ transition language does not allow for the inclusion of small amounts of water.” EX2069 ¶26. She continued that “even very small amounts of water” should not be considered “an ‘impurity ordinarily associated’ with the claimed solution,” and is

thus excluded from the claims—even water “less than about 0.1%.” *Id.* ¶¶26, 33. She proposes that if the claims allow some water—even trace impurities—“a POSA cannot reasonably ascertain what is within the scope of the invention, and what is outside the scope of the invention, and the claims are indefinite.” *Id.* ¶50; *see* EX2050 (Joint-CC Br.) at 55-56; EX2069 ¶¶53, 57.

B. PETITIONER’S CONFLICTING PTAB POSITION FOR “CONSISTING OF”

Meanwhile in this forum, Petitioner’s contentions directly contradict its position in district court in multiple ways. First, Petitioner does not propose here that “consisting of” requires construction. Indeed, Petitioner fails to prove (or even address) whether the formulations of Gwozdz-PCT (EX1009) and Meezan (EX1010) have water, whether trace amounts or otherwise. But as discussed below every prior art formulation on which Petitioner relies does, in fact, contain some water. *See infra* §IX.A.2. Worse yet, Petitioner affirmatively relies on at least one embodiment of Gwozdz-PCT that is in an aqueous solution (i.e., explicitly including water). *See infra* §IX.B.4.b. Petitioner nowhere explains or justifies this inconsistency.

Second, Petitioner contends the claims are indefinite in district court, but here contends that a POSA can understand their scope when asserting obviousness. Petitioner “is *required* to explain why those different positions are warranted.” *Tesla, Inc. v. Intellectual Ventures II LLC*, IPR2025-00340, Paper 18 at 3 (P.T.A.B.

Nov. 5, 2025) (Director Review, informative) (internal citations omitted); *see Cambridge Mobile Telematics, Inc. v. Sfara, Inc.*, IPR2024-00952, Paper 12 at 8 (P.T.A.B. Dec. 13, 2024) (informative) (requiring explanation of inconsistency in claim-construction positions).

Petitioner wholly ignores its district court claim construction to advance its contradictory obviousness arguments here.

V. THE GROUNDS AND ASSERTED REFERENCES

Petitioner asserts the following obviousness grounds and references:

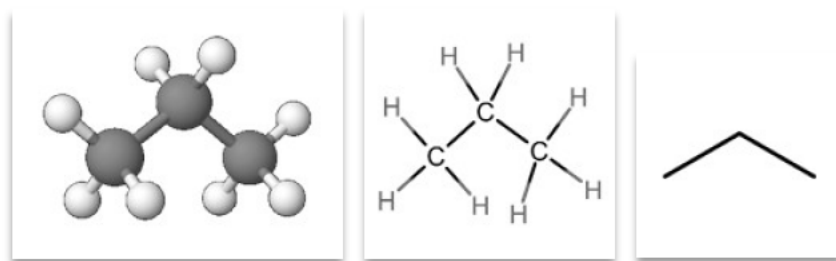
Reference	Asserted Status (pre-AIA)	Ground(s)
WO2009/120933 Gwozdz-PCT (EX1009)	§102(e)(1)	1-3
US2006/0046962 Meezan (EX1010)	§102(b)	1-3
US2008/0279784 Cartt-784 (EX1065)	§102(e)(1)	2
USP23/NF18 (EX1066)	§102(b)	3

VI. TECHNICAL BACKGROUND

Dr. Brown provides a tutorial, excerpted below, covering aspects of organic chemistry and pharmaceutical formulations relevant to this dispute. EX2074 ¶¶63-103; EX2049. Dr. Brown also discusses benzodiazepines, including diazepam. *Id.* ¶¶103-113 (citing EX2062-EX2067, EX2071).

A. ALKANES

Alkanes are a type of hydrocarbon compound that are made entirely of carbon (C) and hydrogen (H) atoms, and in which all the carbon-carbon bonds are single bonds. A three-carbon alkane is propane (C_3H_8). It can be depicted in three-dimensional fashion, in short-hand fashion, or in skeletal fashion:

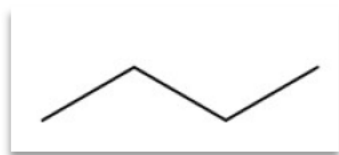


EX2074 ¶¶64-68 (referencing EX2051-EX2052).

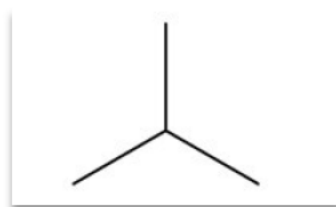
B. ISOMERS: LINEAR AND BRANCHED

Alkanes of four or more carbons can form *isomers*, which are “compounds that have identical formulas but differ in the nature or sequence of bonding of their atoms or in the arrangement of their atoms in space.... In general, isomers have different physical and chemical properties.” EX2051 at 11. These different arrangements lead to distinct biological activity, even though the number and type of atoms are identical. EX2070 at 22:10-23:22, 25:13-25:24; EX2074 ¶69.

A simpler example is butane (C_4H_{10}), which can exist as two isomers:



n-butane



iso-butane

Both isomers have the same number of carbons and hydrogens, but they have different structures. The “*n*-” nomenclature refers to the “normal” isomer, in which all carbons form a continuous, unbranched (**linear**) chain: “Straight-chain alkanes are called **normal alkanes**, or simply ***n*-alkanes**, to distinguish them from the branched alkanes...” EX2051 at 9.

[S]traight-chain alkanes (also called normal alkanes, or *n*-alkanes) ... consist of chains of carbon atoms bonded to one another by single bonds ... [which] have the generic formula C_nH_{2n+2} .

EX2052 at 8. In contrast to *n*-alkanes, the other type of isomer is **branched**:

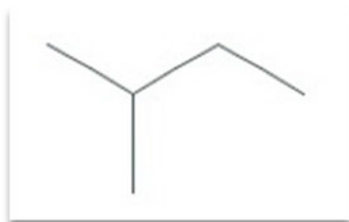
Branched-chain alkanes are hydrocarbons that contain only C—C and C—H single bonds but in which the carbon atoms are no longer arranged in a straight chain. One or more carbon atoms in each molecule are bonded to three or four other carbon atoms rather than to only one or two as in the normal alkanes or cycloalkanes.

EX2052 at 9; EX2074 ¶70.

Butane has two isomers, but as the number of carbons increases, the number of isomers grows. For example, pentane (C_5H_{12}) has one linear and two branched isomers:



n-pentane



iso-pentane



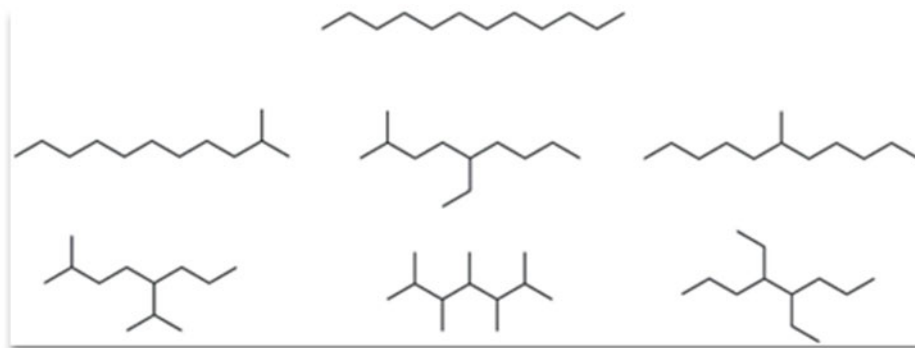
neo-pentane

Larger alkanes can exist in many more isomeric structures, as shown below.

TABLE 3.3 Number of Isomers of C_nH_{2n+2}

n	Number of Isomers
4	2
5	3
6	5
7	9
8	18
9	35
10	75
12	355
15	4,347
20	366,319

EX2051 at 11. A handful of the 355 isomers of dodecane ($C_{12}H_{26}$) include:



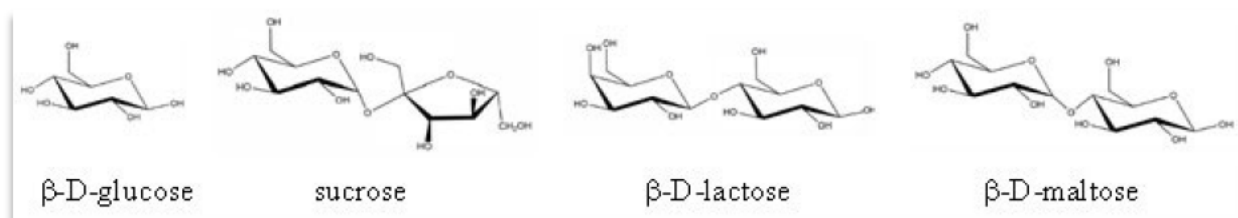
n-dodecane is the linear isomer depicted at the top of this figure. Other than *n*-dodecane, every other isomer of dodecane is branched in one or more locations.

EX2074 ¶¶71-72.

When an alkane is not a standalone molecule, but is instead bonded to another chemically distinct portion of a molecule (often called a *moiety*), the “group name is derived by replacing the *-ane* of the corresponding alkane by the suffix *-yl*.”² EX2051 at 10. For example, dodecane becomes “dodecyl.” EX2074 ¶73.

C. SACCHARIDES AND GLYCOSIDES

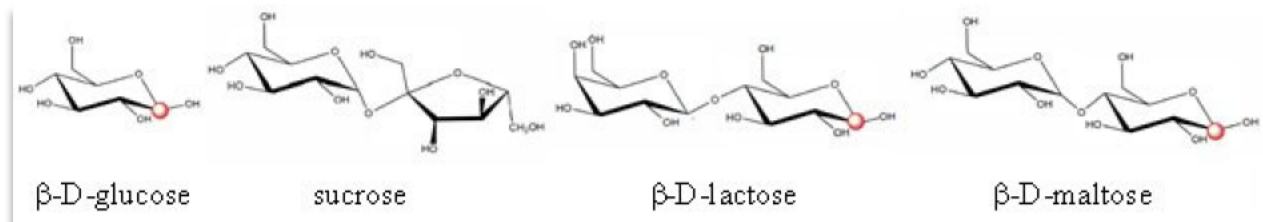
One category of carbohydrates is commonly called “sugars,” or “saccharides.” A simple sugar molecule with one unit (monosaccharide) has the chemical formula of $C_6H_{12}O_6$ (e.g., glucose). Exemplary disaccharides (two units) include sucrose, lactose, and maltose:



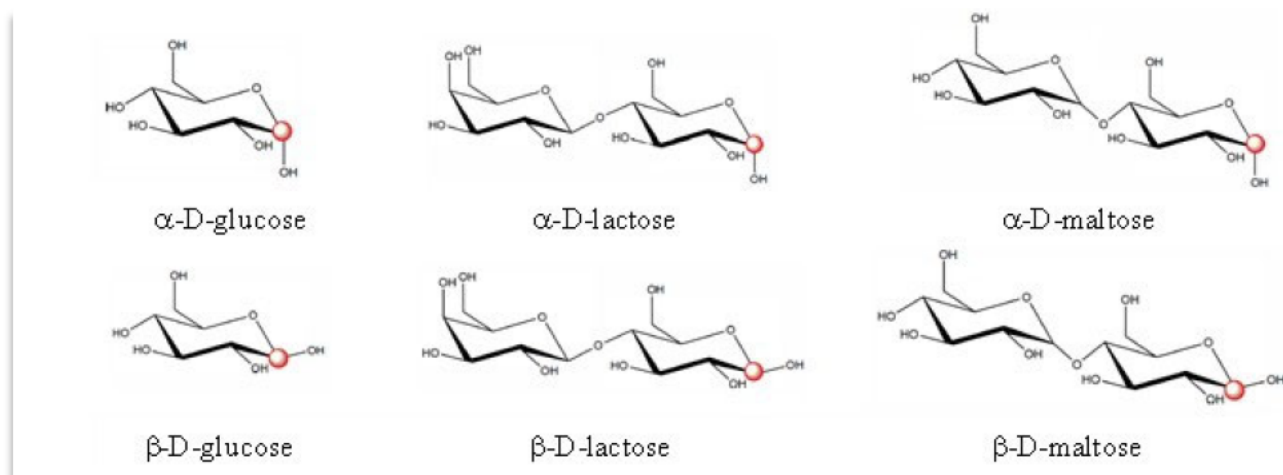
EX2051 at 13-15; EX2074 ¶¶74-75.

² Chemical bonding of an alkyl group to another moiety can result in additional structural isomers, depending on which position of the alkyl group bonds with the other moiety. EX2074 ¶73.

Like alkanes, saccharides isomerize, and can take on different structural forms while maintaining the same chemical composition. Anomers are isomers of saccharides that differ in the 3-dimensional configuration of the “anomeric carbon,” indicated in red.



EX2051 at 13-14. If the -OH group on the anomeric carbon is on an opposite “face” of the ring in relation to the -CH₂OH (*trans* configuration), the saccharide is termed the α -anomer. If those two groups are on the same “face” (*cis* configuration), the saccharide is termed the β -anomer, as shown below.

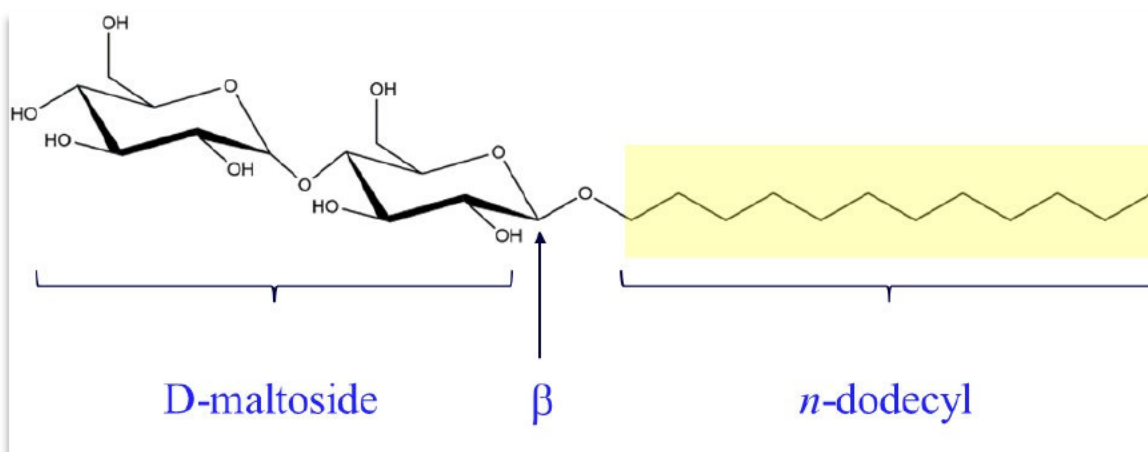


EX2051 at 13-15. When a saccharide is chemically connected to another chemically distinct moiety, the resulting molecule is often termed a “*glycoside*.” For example,

when connected to another moiety, maltose becomes “maltoside.” EX2051 at 13-15; EX2074 ¶¶74-81.

D. N-DODECYL-BETA-D-MALTOSIDE AND DODECYL MALTOSIDE

The compound *n*-dodecyl-beta-D-maltoside (also known as lauryl-beta-D-maltoside or *n*-dodecyl- β -D-maltoside) has a specific chemical structure and resulting functional characteristics:



n-dodecyl-beta-D-maltoside has a specific sugar and stereochemistry (D-maltose), dodecyl isomer (*n*-dodecyl, a linear chain), and anomeric carbon (β). “Dodecyl maltoside” is a broader genus that includes at least 1,420 compounds (355 isomers of dodecyl x 2 isomers of maltose x 2 anomeric isomers), plus more if the maltoside moiety is bonded to carbons 2-11 of the dodecyl moiety. EX2074 ¶81.

VII. GWOZDZ-PCT (EX1009) IS NOT §102(e) PRIOR ART

“In an *inter partes* review, the burden of persuasion is on the petitioner to prove ‘unpatentability by a preponderance of the evidence,’ 35 U.S.C. §316(e), and

that burden never shifts to the patentee.” *Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). This rule “necessarily requires the reference patent document first to be qualified as prior art.” *Intelligent Wellhead Sys., Inc. v. Downing Wellhead Equip., LLC*, IPR2024-00256, Paper 11 at 10-11 (P.T.A.B. June 5, 2024). “The burden to make this showing thus falls squarely on Petitioner.” *Id.* at 12. Petitioner cannot meet its burden to demonstrate that Gwozdz-PCT (EX1009) qualifies as prior art.

First, the ’786 Patent traces priority to March 28, 2008, the same day Gwozdz-Provisional (EX1064) was filed. Thus, Gwozdz-PCT is not “before” the application date of the ’787 Patent and does not qualify as Section 102(e) prior art.

Second, every named inventor on Gwozdz-PCT (Gwozdz, Loxley, and Mitchnick) is also named on the ’786 Patent. Petitioner has not addressed (much less demonstrated) the “by another” requirement of Section 102(e). *See Duncan Parking Techs., Inc. v. IPS Grp., Inc.*, 914 F.3d 1347, 1358 (Fed. Cir. 2019) (describing factors to analyze Section 102(e)); *Google LLC v. IPA Techs. Inc.*, 34 F.4th 1081, 1085 (Fed. Cir. 2022) (applying *Duncan* to an obviousness challenge).

A. THE ’786 PATENT CLAIMS HAVE PRIORITY TO THE MARCH 28, 2008 PROVISIONAL

Petitioner does not dispute that the challenged claims have priority to the first non-provisional, 12/413,439, filed March 27, 2009. *See* Pet. at 12, 16, 23, 25

(repeatedly referring to, but not challenging, the “March 27, 2009” priority date). Dr. Donovan agreed that she “offered no opinion that any claim of the [’786 Patent] is entitled to a priority date after March 27, 2009.” EX2070 at 216:8-17. The disclosures in the specifications are continuous across the non-provisional applications. *See* EX2048, EX2060 (redline comparisons); EX2074 ¶¶124-188 (tracing support through the non-provisional applications). The sole dispute is whether the ’786 Patent can trace priority one step further up the chain, to the ’558 Provisional filed March 28, 2008.

The only argument Petitioner raises in this regard is a purported lack of written description support in the ’558 Provisional for “*n*-dodecyl beta-D-maltoside.” Pet. at 12-16. Petitioner spends over four pages arguing why “alkyl glycosides” (the genus) is not disclosed (Pet. at 12-16), but the ’786 Patent claims do not require “alkyl glycoside.” The ’786 claims require a specific chemical compound, *n*-dodecyl-beta-D-maltoside, and the Petition addresses that in one conclusory sentence buried at the end. *Id.* at 16.³ Petitioner is wrong.

³ “Ultimately, it is petitioner’s burden to present a clear argument.” *Netflix, Inc. v. DIVX, LLC*, 84 F.4th 1371, 1377 (Fed. Cir. 2023) (“Board should also not have to decode a petition to locate additional arguments beyond the ones clearly made”).

1. **The '558 Provisional Properly Incorporates the Sigma Catalog**

The '558 Provisional states, “[E]nhancing agents that are appropriate include ... biological detergents listed in the SIGMA Catalog, 1988, page 316-321 (which is incorporated herein by reference).” EX1008 ¶[152] (emphasis added).⁴ This is a proper incorporation by reference of the six pages of the Sigma catalog, which “identif[ies] with detailed particularity what specific material it incorporates and clearly indicate[s] where that material is found in the various documents.” *See Zenon Envtl., Inc. v. U.S. Filter Corp.*, 506 F.3d 1370, 1378 (Fed. Cir. 2007). Every non-provisional application leading up to the '786 Patent expressly states this exact language incorporating the Sigma Catalog. EX1039 ('439 Application) ¶[0139]; EX1005 ('397 Application) ¶[0139]; EX1002 ('786 FH) at 587 ¶[0139]. This is a proper use of incorporation. Rather than “repeating some information contained in another document,” the effect of the incorporation is that the “information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed.

⁴ It is undisputed that the '786 Patent and its non-provisional parent applications properly reference the '558 Provisional. 35 U.S.C. §120; 37 C.F.R. §1.78(a)(3). The remaining requirements of Rule 1.78 are met, and Petitioner does not contend otherwise.

Replacing the identified material incorporated by reference with the actual text is not new matter.” M.P.E.P. §2163.07(b).

The Sigma catalog (EX1026) was a well-known reference that a POSA would have had at hand. EX2074 ¶¶190-191. Dr. Donovan herself was familiar with the Sigma catalog, as it was “widely distributed amongst researchers in the field” and the compounds it lists were available to purchase. EX2070 at 151:1-152:4, 179:8-12.

2. The '558 Provisional Is Entitled to Incorporate the Sigma Catalog

Citing 37 C.F.R. §1.57(d), Petitioner contends that because it is “non-patent literature,” Neurelis “cannot rely on the incorporation by reference of the Sigma Catalog in the '558 Provisional to assert that the ‘*n*-dodecyl beta-D-maltoside’ limitation is supported by the disclosure [of the] '558 Provisional.” Pet. at 15.

First, Neurelis notes that provisional applications are not subject to any rules of examination and need not include any patent claims. *See* 35 U.S.C. §111(b). Thus, whether a provisional *itself* incorporates materials that could be considered “essential” is irrelevant. *See* 37 C.F.R. §1.57(d)(1); *see Samsung Electronics. Co. v. Acqis LLC*, IPR2021-00608, Paper 10 at 12 (P.T.A.B. Dec. 8, 2021) (“whether certain disclosure is ‘essential’ depends entirely on what the claims recite in the

particular application, not the claims in the later-filed application as Petitioner alleges”).

Second, the purpose of a provisional application is to “to enable domestic applicants to quickly and inexpensively file provisional applications” and to later “claim the benefit of priority in a given application in the United States.” *See* M.P.E.P. §201.04(III). Here, every subsequent non-provisional application incorporates by reference both the ’558 Provisional and the Sigma catalog solely for purposes of priority, and the statutes do not restrict what the priority materials can incorporate:

The limitations on the material which may be incorporated by reference in U.S. patent applications which are to issue as U.S. patents do not apply to applications relied on only to establish an earlier effective filing date Neither 35 U.S.C. 119(a) nor 35 U.S.C. 120 places any restrictions or limitations as to how the claimed invention must be disclosed in the earlier application to comply with 35 U.S.C. 112(a). Accordingly, an application is entitled to rely upon the filing date of an earlier application, even if the earlier application itself incorporates essential material by reference to another document. *See Ex parte Maziere*, 27 USPQ2d 1705, 1706-07 (Bd. Pat. App. & Inter. 1993).

M.P.E.P. §608.01(p)(I)(B). When a parent application incorporates essential material by reference, “all of the subject matter in [that] reference is present in the parent application.” *Ex Parte Nebrigic*, Appeal 2014-006607, 2016 WL 949023, at *2 (P.T.A.B. Mar. 10, 2016). When the descendant application claims priority back

to the parent application under §120, “there is no issue of improper ‘double incorporation’ of essential subject matter” that violates 37 C.F.R. §1.57(d). *Id.*

Thus, the ’558 Provisional’s incorporation of material from a well-known catalog is proper, and subsequent incorporations in the chain of non-provisional applications do not violate Rule 1.57. Accordingly, the ’786 Patent claims priority not only to 2009 (which is undisputed), but also to the ’558 Provisional in 2008.

3. The ’558 Provisional Provides Written-Description Support for the Challenged Claims

The Board preliminarily held that even if the ’558 Provisional included the Sigma catalog excerpt, it provides insufficient written description support for the challenged claims because there was an “[insufficient] disclosure of ‘blaze marks’ in the ’558 Provisional” to show possession of “n-dodecyl beta-D-maltoside.” Paper 13 at 29. As explained below, this is not a “blaze marks” case and, in any event, sufficient guidance is present.

a. The ’558 Provisional Discloses the Claim Language Verbatim, Directing a POSA to *n*-dodecyl- β -D-maltoside

The Sigma catalog excerpt incorporated by reference in the ’558 Provisional (and each subsequent non-provisional application) specifies “*n*-dodecyl β -D-maltoside” on the first cited page and shows it was commercially available:

BIOLOGICAL DETERGENTS

Sigma offers a wide range of detergents useful to the biochemist for the solubilization of proteins and membrane components. This section is organized into the four major detergent categories:

n-Decyl β -D-glucopyranoside
Digitonin
n-Dodecyl β -D-glucopyranoside
n-Dodecyl β -D-maltoside
n-Heptyl β -D-glucopyranoside
n-Octyl β -D-glucopyranoside
n-Octyl α -D-glucopyranoside
Nonidet P-40
n-Nonyl β -D-glucopyranoside
Triton X-100

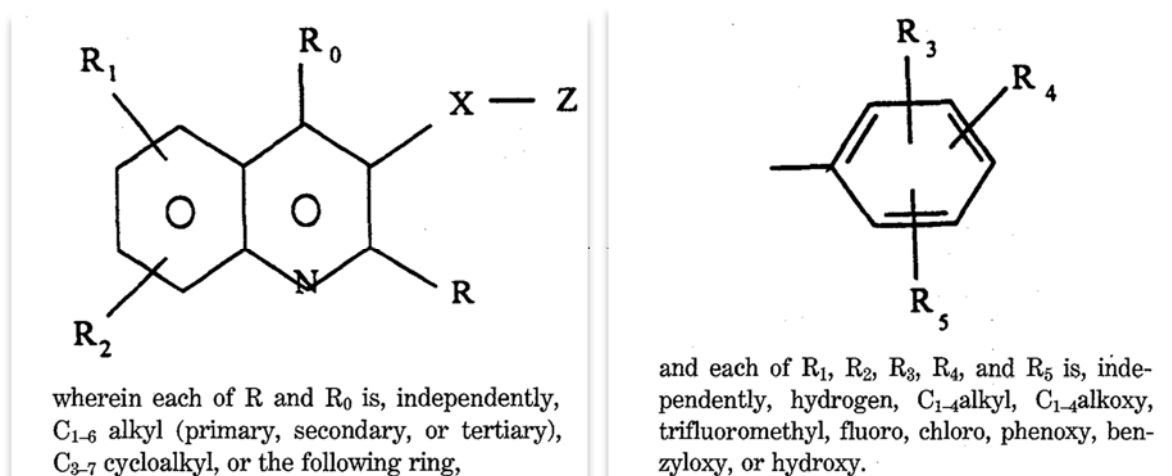
EX1026, 19. The '558 Provisional provides written description support for *n*-dodecyl- β -D-maltoside (the material incorporated by reference) by providing its specific “chemical name.” See *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010) (*en banc*) (“adequate written description requires a precise definition, such as by structure, formula, **chemical name**, physical properties, or other properties ... sufficient to distinguish” the subject matter) (emphasis added). That is, the *n*-dodecyl- β -D-maltoside claim element of the '786 Patent is “directly supported *in haec verba* by the disclosure,” so it “therefore cannot be ... that the inventors did not have possession” of the invention. See *Allergan USA, Inc. v. MSN Lab'ys Priv. Ltd.*, 111 F.4th 1358, 1374 (Fed. Cir. 2024). Even Dr. Donovan agrees a POSA “would immediately discern that this is the same compound that is included in the claims of the '414 Patent.” EX2070 at 178:9-179:7 (the '414 is a child of the '786 Patent and recites the same “*n*-dodecyl beta-D-maltoside” limitation).

In addition to *in haec verba* support, the '558 Provisional discloses other pointers to this portion of the Sigma catalog, including absorption enhancers in dependent claim 35. EX1008 at 40 (“at least one additional ingredient [is] ... enhancers”). “Enhancer” is defined in the '558 Provisional specification as “any material which acts to increase absorption across the mucosa and/or increase bioavailability,” and the specification also describes categories of enhancing materials and agents, including those in the Sigma catalog. *Id.* ¶¶[150]-[152]. The '558 Provisional and the Sigma catalog direct a POSA where to look to arrive at the claimed *n*-dodecyl- β -D-maltoside. EX2074 ¶¶190-195.

b. “Blaze marks” Are Inapplicable

Though not argued by Petitioner, the Board cites “blaze marks” cases for the proposition that “the Federal Circuit rejected the notion that a listing of elective portions of the claimed subject matter was necessarily sufficient to describe the claim as whole.” Paper 13 at 27-28 (citing *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996) and *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326–27 (Fed. Cir. 2000)). A traditional “blaze marks” case, however, is one “in which the claims recite a species where the specification describes only a genus.” *See Allergan*, 111 F.4th at 1372 (distinguishing *Fujikawa* and *Purdue*). Here, the '786 Patent supports a claimed species with disclosure of that exact species. There is no genus and no need for blaze marks.

Fujikawa involved an interference proceeding, with the junior party seeking “to add a sub-genus count to the interference,” and the Federal Circuit addressed whether the senior party’s application supported the proposed count. *Fujikawa*, 93 F.3d at 1569. The senior party’s application disclosed a chemical structure with multiple R groups (depicted below), where each R group could be substituted for a different chemical compound. *Id.* at 1570.



The Court held that disclosure of one species (“cyclopropyl as one possible moiety for R”) “does not mean there is *ipsis verbis* support for every species or sub-genus that chooses that moiety.” *Id.* at 1571. The court rejected a proposed “sub-genus count,” because “simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to particular species or subgenuses” that were not otherwise disclosed. *Id.* The ’786 Patent, in contrast, does not claim a genus or a sub-genus of compounds; it claims one species (*n*-dodecyl-β-D-maltoside), and that very species is disclosed “*ipsis verbis*” in the ’558 Provisional.

See Allergan, 111 F.4th at 1372 (distinguishing *Fujikawa* when “[t]he claims are narrow” and “recite specific ingredients ... not classes of ingredients”).

Purdue Pharma is also inapplicable. There, the claims recited “the $C_{\max}/C_{24}$ ratio” of “more than two.” *Purdue Pharma*, 230 F.3d at 1324. The specification contained exemplary ratios of both “greater than two” and “less than two.” *Id.* at 1326. The court found no written description, because the patent disclosed “a multitude of pharmacokinetic parameters, with no blaze marks directing the skilled artisan to the [claimed] ratio or what value that ratio should exceed.” *Id.* Again, a claim to a large genus (ratio “greater than two” with an unbounded maximum) was found insufficiently supported by a few examples in the specification.

The '786 Patent “is not a ‘blaze marks’ case in which the claims recite a species where the specification describes only a genus.” *See Allergan*, 111 F.4th at 1372. The specification identifies the claimed species (*n*-dodecyl- β -D-maltoside) as an example among a finite list of compounds classified as biological detergents, within the appropriate unclaimed genus of enhancing agents. EX1026 at 19. This limited disclosure is not a laundry list of millions of items or a generic Markush disclosure, as in *Fujikawa* or *Purdue Pharma*. *See Allergan*, 111 F.4th at 1374-75 (“[T]his is not a case in which the disclosure provides only a ‘broad outline of a genus’s perimeter,’ and claims a species within that broad outline. ... Nor do the disclosures ... provide ‘thousands’ of possible formulations from a ‘laundry list of

ingredients.””). Blaze marks are not required when the disclosure provides the exact species that is claimed.

B. GWOZDZ-PCT IS NOT ENTITLED TO ITS PRIORITY DATE

Another, independent reason that Gwozdz-PCT is not prior art is because it was filed March 27, 2009, the same day as 12/413,439 (parent to '786 Patent), and Gwozdz-PCT cannot trace priority to 61/040,281. Thus, regardless of whether the '786 Patent achieves priority to 61/040,558, the priority of Gwozdz-PCT is not earlier.

For Gwozdz-PCT to achieve a §102(e) (pre-AIA) prior art date to the 61/040,281 provisional, two requirements must obtain. First, Petitioner must demonstrate that the provisional provides written-description support for at least one claim. *See Dynamic Drinkware*, 800 F.3d 1375, 1382 (Fed. Cir. 2015). Second, “the cited content” relied on to support the unpatentability analysis must be “adequately supported by the written description of the provisional application.” *In re Riggs*, 131 F.4th 1377, 1384-85 (Fed. Cir. 2025). Both factors are required.

Petitioner fails to meet the second factor. Petitioner asserts that “a motivation existed to combine the teachings of Meezan related to alkyl glycosides with the pharmaceutical solutions described in Gwozdz.” Pet. at 29. The basis is that “Gwozdz teaches that the pharmaceutical solutions ... may further incorporate additional pharmaceutically acceptable additives to improve the efficacy.” *Id.*

(citing EX1009, 10:12-16); EX2070 at 78:22-79:6. As the Board explained, however:

Petitioner did not establish that Gwozdz's disclosure of "penetration enhancers" finds support in the Gwozdz Provisional. Pet. 22. Conversely, Patent Owner shows that the phrase is absent in the Gwozdz Provisional. Prelim. Resp. 37

Paper 13 at 35. This omission can be seen by comparing identical paragraphs from the two documents.

10 solubilizing agent such as Cremophor. Such pharmaceutical compositions may further contain other pharmaceutically acceptable additives such as, but not limited to, acidifying, alkalizing, buffering, chelating, complexing and solubilizing agents, antioxidants and antimicrobial 15 preservatives, humectants, suspending and/or viscosity modifying agents, tonicity and wetting or other biocompatible materials.	EX1064, 10:10-17
10 compositions may further contain other pharmaceutically acceptable additives such as, but not limited to, acidifying, alkalizing, buffering, chelating, complexing and solubilizing agents, antioxidants and antimicrobial preservatives, penetration enhancers, humectants, suspending 15 and/or viscosity modifying agents, tonicity and wetting or other biocompatible materials.	EX1009, 10:10-17

There is no disclosure of "penetration enhancers" in Gwozdz-Provisional (EX1064); EX2074 ¶247. This subject matter is not prior art.

Notably, Petitioner has not reconciled how it can simultaneously argue that Gwozdz-Provisional provides written-description support for penetration enhancers

(when that subject matter is absent from the document) but that the '558 Provisional lacks written-description support for a claimed species (when there is verbatim disclosure).

C. IMPROPER GROUND UNDER SECTION 311

Gwozdz-PCT and Cartt-784 are unavailable to be used as asserted references in an IPR proceeding, which is limited to “prior art consisting of patents or printed publications.” 35 U.S.C. §311(b). They are not patents, and Section 311(b) does not include “patent applications” under the available grounds. They are also not “printed publications” in the sense that “before the critical date the reference must have been sufficiently accessible to the public interested in the art.” *See Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1568 (Fed. Cir. 1988). Gwozdz-PCT and Cartt-784 each published after the '786 Patent's critical date.⁵

VIII. GWOZDZ-PCT IS NOT AVAILABLE IN AN OBVIOUSNESS COMBINATION UNDER 35 U.S.C. §103(c)(2)

Gwozdz-PCT cannot form the basis of an obviousness challenge under §103(c) (pre-AIA). The inventions claimed in the '787 Patent resulted from a qualifying joint research agreement (JRA) that was in effect when the inventions

⁵ The Federal Circuit “conclude[d] that §§311(b) and 102(e)(1) permit IPR challenges based upon published patent applications.” *Lynk Labs, Inc. v. Samsung Elecs. Co.*, 125 F.4th 1120, 1132 (Fed. Cir. 2025). Lynk Labs has sought *certiorari* from the Supreme Court, so Neurelis includes the argument to preserve it.

were made, the inventions were developed within the scope of that agreement, and the patent is in the process of being properly amended to disclose the parties to the agreement.

Section 102(e) prior art does not preclude patentability if, at the time the invention was made, the prior art and the claimed invention were deemed to be owned by the same entity or subject to an obligation of assignment to that entity.

This exemption applies when:

- 1) The claimed invention was made by or on behalf of parties to a joint research agreement that was in effect on or before the claimed invention was made;
- 2) The claimed invention was made as a result of activities undertaken within the scope of the joint research agreement; and
- 3) The application for patent for the claimed invention discloses or is amended to disclose the names of the parties to the joint research agreement.

35 U.S.C. §103(c)(2)(A)-(C). All three conditions apply here.

As explained below, Particle Sciences, Inc. (“PSI”) and Questcor Pharmaceuticals, Inc. (“Questcor”) entered into a JRA before the ’786 Patent’s earliest claimed priority date. PSI is the assignee of Gwozdz-PCT, and Questcor is

the predecessor-in-interest of the '786 Patent.⁶ The claimed inventions arose from activities conducted within the scope of that JRA, and the '786 Patent is in the process of being amended to identify the parties to the JRA. *See* Papers 23, 26. Thus, Gwozdz-PCT is unavailable for obviousness.

A. FACTOR 1: THE '786 PATENTED INVENTIONS WERE MADE BY OR ON BEHALF OF QUESTCOR AND PSI, WHO WERE PARTIES TO A JRA THAT WAS IN EFFECT BEFORE THE CLAIMED INVENTIONS WERE MADE

A JRA was in effect before the earliest priority document, the '558 Provisional, was filed on March 28, 2008. *See* 35 U.S.C. §103(c)(3).

1. Questcor and PSI's Joint Research Agreement

In late 2006, Questcor approached PSI to help with research and development work that resulted in the inventions claimed in the '786 Patent. As part of that process, the parties executed a Master Services Agreement ("MSA"), dated April 1, 2007. EX2030. The MSA formalized Questcor's and PSI's partnership and outlined the scope of collaboration to perform formulation work for the diazepam nasal-spray development program that is the subject of the '786 Patent. EX2030 at 1.

⁶ Questcor sold its interest in the JRA to Hale BioPharma Ventures ("HBV") in 2008. *See* EX2047 (Hale Decl.) ¶10. HBV is the predecessor in interest to Neurelis, Inc., the Patent Owner.

The MSA demonstrates the existence of a JRA under Section 103(c), because it is a written contract executed by two or more parties for the performance of experimental, developmental, or research work in the field of the invention. *See* 35 U.S.C. §103(c)(3) (pre-AIA). Additional documents, communications, and experimental details that were shared between the parties provide further evidence that a JRA existed between Questcor and PSI. *See id.*; EX2032 (H.R. Rep. No. 108-425) at 10 (“Congress does not intend to prescribe the specific form of the agreement parties must use to benefit from this Act nor to require the writing be contained in a single instrument.”); EX2033 (150 Cong. Rec. S7520-05) at 3 (Sen. Hatch, “The House indicated in its committee report that a joint research agreement may be evidenced by one or more writings.”); EX2035; EX2037; EX2040.

2. The '558 Provisional Was Filed on March 27, 2008

Almost one year after signing the MSA, Questcor filed the '558 Provisional pursuant to the terms of the MSA. The '558 Provisional identifies individuals from Questcor and PSI who worked jointly to develop the inventions disclosed therein. *See generally* EX2045-EX2047 (inventor declarations). Gwozdz-Provisional (61/040,281), filed the same day pursuant to the JRA, identifies the same PSI individuals who worked jointly to develop the inventions disclosed in the '558 Provisional.

3. Assignment of the JRA to HBV and Subsequently to Neurelis

In June 2008, Questcor transferred all its interest and rights to the JRA and the QSC-002 Project, including the inventions claimed in the '786 Patent, to HBV pursuant to an Asset Purchase Agreement dated June 27, 2008. *See* EX2031 (APA). The JRA between Questcor and PSI was expressly assigned to HBV. *See id.* at 2 [REDACTED] (assigning the MSA from Questcor to HBV).

In December 2018 and February 2019, Neurelis was assigned all the QSC-002 Project assets, including the '786 Patent and the patent applications to which it claims priority, as assignments recorded in the PTO's assignment database show. Reel/Frame Nos. 48211/0840, 48271/0304, 58369/0292, and 58369/0412.

4. The Inventions Were Made by the Parties to the JRA

As the declarations of inventors Cartt, Mitchnick, and Hale elaborate (EX2045-EX2047), the parties to the JRA each contributed to the formulations that the '786 Patent now claims. All the work was done and performed under the JRA. Even before the '558 Provisional was filed, the parties worked to obtain supplies of and technical knowhow concerning *n*-dodecyl- β -D-maltoside (Ed Maggio at Aegis, Inc.). EX2041 (Letter Agreement); EX2034; EX2036; EX2038; EX2042; EX2044; *see* EX2061 (Ward) at 4 (discussing Intravail). Neurelis ultimately signed that

supply and license agreement as part of the diazepam nasal-spray development program under the JRA. EX2043 (License Agreement).

B. FACTOR 2: THE CLAIMED INVENTIONS WERE MADE AS A RESULT OF ACTIVITIES UNDERTAKEN WITHIN THE SCOPE OF THE JRA

The '786 Patent inventions resulted from activities undertaken within the scope of the JRA. As Cartt (Questcor) and Mitchnick (PSI) testified, the MSA governed the development of the diazepam nasal-spray development program. EX2045 ¶19; EX2046 ¶14. This agreement formalized Questcor's engagement of PSI (along with HBV and Neurelis, as Questcor's successors in interest) to perform formulation work for nasal spray products targeting central nervous system disorders, outlining the scope and purpose of the collaboration as follows:

[REDACTED]

[REDACTED]

[REDACTED]

EX2030 at 1.

After executing the MSA, Questcor and PSI continued to collaborate to develop the claimed invention of the '786 patent. *See generally* EX2045-EX2047. The MSA provided that Questcor retained ownership of all intellectual property for inventions [REDACTED]

[REDACTED]. EX2030 at 3 [REDACTED]; *accord id.* at

1 [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] *See* EX2030 at 3; *see* EX2045 ¶26.

Pursuant to this arrangement, Questcor and PSI filed two separate patent applications on March 28, 2008. *See* EX2040. These filings became the '558 Provisional (owned by Questcor) and Gwozdz-Provisional (owned by PSI). *See id.*

Shortly thereafter, Questcor assigned the joint research agreement to HBV, [REDACTED]
[REDACTED]. EX2030 at 5. In June 2008, Questcor sold the diazepam nasal-spray project to HBV via an Asset Purchase Agreement, [REDACTED]

[REDACTED] [REDACTED]

[REDACTED]

[REDACTED] HBV continued the collaboration with PSI under the same agreement, ultimately filing the '439 Application (parent of the '786 Patent).

The collaborative efforts under the MSA resulted in the filing of both the '558 Provisional and Gwozdz-Provisional on March 28, 2008, and continued through the filing of the '439 Application on March 27, 2009 (to which the '786 Patent claims priority) and Gwozdz-PCT. These filings were direct outcomes of the formulation and development work contemplated by the MSA, as evidenced by the declarations of Cartt, Mitchnick, and Hale, as well as contemporaneous documentation.

Accordingly, the claimed invention was developed squarely within the scope of the JRA, satisfying the second prong of §103(c)(2).

C. FACTOR 3: THE '786 PATENT IS BEING AMENDED TO DISCLOSE THE NAMES OF THE PARTIES TO THE JRA

Pursuant to 37 C.F.R. §1.71(g)(1), the specification may be amended to include the names of the parties to a joint research agreement. Neurelis has requested leave to seek a certificate of correction from the Director to identify Questcor, HBV, and PSI as parties to the joint research agreement underlying the claimed invention. Paper 26. Before the time for Final Written Decision, Neurelis expects that the Director will have granted the request and issued the certificate of correction, thus satisfying the third prong of §103(c)(2).

IX. GROUND 1-3: THE CHALLENGED CLAIMS ARE NOT OBVIOUS OVER GWOZDZ-PCT AND MEEZAN

Petitioner's obviousness contentions should be rejected outright, because Petitioner has not "carried its burden to prove that all claimed limitations are

disclosed in the prior art.” *PAR Pharm.*, 773 F.3d at 1194. Petitioner and Dr. Donovan fail to address an element of every challenged claim: *n*-dodecyl- β -D-maltoside. In view of this fundamental hole in the Petition, the Board need not “consider motivation to combine and reasonable expectation of success.” *Id.*

A. THE COMBINATION DOES NOT DISCLOSE ALL CLAIM LIMITATIONS

The Director has stated that the USPTO “will enforce and no longer waive the requirement of 37 C.F.R. §42.104(b)(4) (Rule 104(b)(4)) that a petition for inter partes review (IPR) ‘must specify where each element of the claim is found in the prior art patents or printed publications relied upon.’” *See* Director Memo (7/31/2025).⁷ Although “expert testimony ... and other ... general knowledge” may have previously sufficed to “supply a missing claim limitation” (*id.*), the Petition here lacks even that.

1. “*n*-dodecyl beta-D-maltoside”

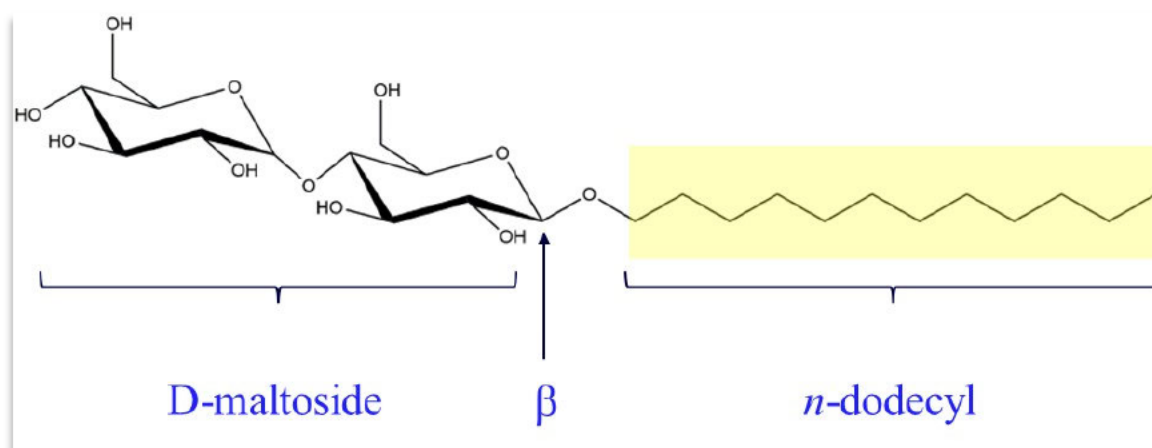
The asserted prior art does not disclose the specific compound recited in every challenged claim: “*n*-dodecyl beta-D-maltoside.”

⁷ https://www.uspto.gov/sites/default/files/documents/aapa_memo_final__signed.pdf.

I. A pharmaceutical solution for nasal administration consisting of:
 a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof;
 one or more natural or synthetic tocopherols or tocotrienols selected from the group consisting of α -tocopherol, β -tocopherol, γ -tocopherol, δ -tocopherol, α -tocotrienol, β -tocotrienol, γ -tocotrienol, δ -tocotrienol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w);
 one or more alcohols in an amount from 10% to 70% (w/w), wherein the one or more alcohols comprises benzyl alcohol; and
 n-dodecyl beta-D-maltoside.

II. A pharmaceutical solution for nasal administration consisting of:
 a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof;
 one or more natural or synthetic α -tocopherols selected from the group consisting of tocopherol, β -tocopherol, γ -tocopherol, δ -tocopherol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w);
 one of more alcohols in an amount from 10% to 70% (w/w), wherein the one or more alcohols comprises benzyl alcohol; and
 n-dodecyl beta-D-maltoside.

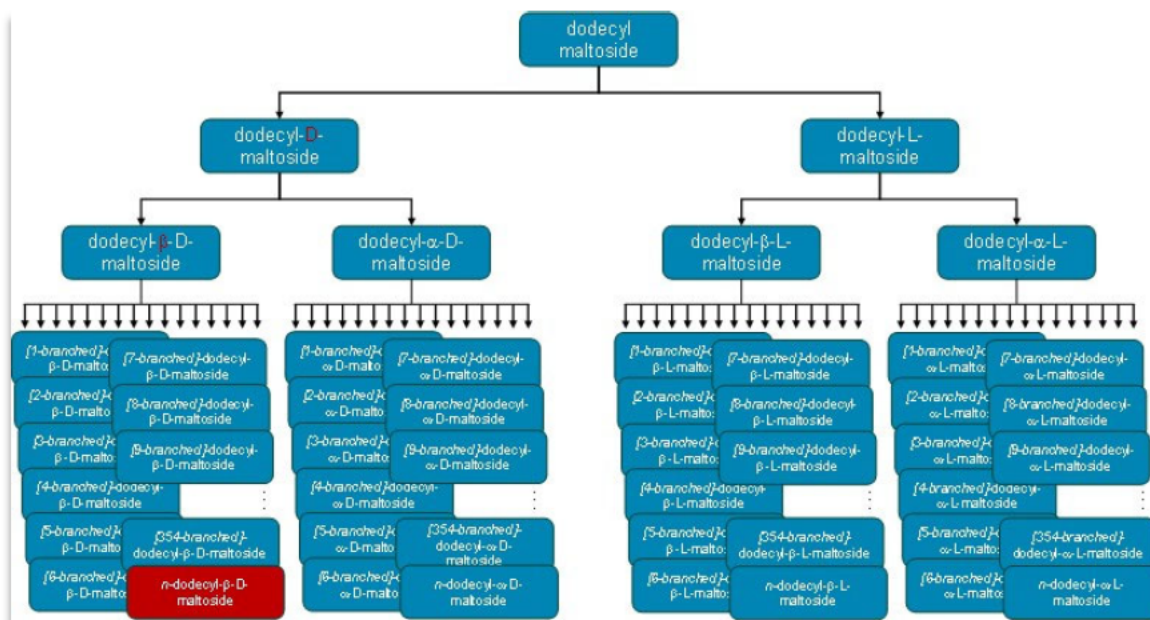
This compound is shown below, with the “n-dodecyl” moiety highlighted:



EX2074 ¶¶68-70, 81; *see supra* §VI (describing the “n-” prefix).

Gwozdz-PCT (EX1009) does not disclose n-dodecyl-beta-D-maltoside, and Petitioner does not contend otherwise. Pet. at 40-42, 52. Rather, Petitioner relies on Meezan (EX1010). Yet Petitioner does not point to any disclosure in Meezan of “n-dodecyl beta-D-maltoside.” Every mention in the Petition of this limitation is to the sub-genus, “dodecyl beta-D-maltoside” (with 355 species), or the genera “dodecyl maltoside” (over 700 species) or “alkyl glycoside” (countless species). *See* Pet. at 27-29, 31-33, 41-42; EX2074 ¶¶217-222. As described above in the Technology

Background, “dodecyl” (12 carbons) “maltoside” (linked to maltose) is one subgenus of “alkyl glycosides.” Within the subgenus of “dodecyl maltoside,” there are hundreds of species.



EX2074 ¶¶68-81, 223, 272. The Petition is completely silent on any disclosure or teaching in the prior art of the claimed compound, “*n*-dodecyl beta-D-maltoside.” This omission alone suffices to reject Petitioner’s obviousness assertions. *PAR Pharm.*, 773 F.3d at 1194 (citing *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1164 (Fed. Cir. 2006) (considering motivation to combine only “if all the elements of an invention are found in a combination of prior art references”)).

Petitioner should not be allowed to backfill this hole in its Reply brief through expert declaration or otherwise. *See* 37 C.F.R. §42.104(b)(4) (“petition must specify where each element of the claim is found in the prior art”); 35 U.S.C. §312(a)(3)-

(a)(4) (similar). Nor can it, as its expert Dr. Donovan conceded that she did not know what “*n*-” means in the recited claims.

Q. Do you have an understanding of what that “*n*” prefix means in the context of n-Dodecyl-beta-D-maltoside?

A. It’s a structural arrangement indicator that escapes me at the moment.

Q. If I told you it it’s an indicator that stands for “normal,” would that make sense?

A. [I]t makes sense because it’s in keeping that I know ... that’s what “*n*” stands for, but what “normal” is being attributed to is where I – I’m not willing to state that I know that clearly right now.

Q. You don’t recall what structural information the “*n*” conveys in n-Dodecyl-beta-D-maltoside; is that correct?

A. Not at this moment to testify to.

EX2070 at 193:2-25. Given her sworn testimony, it is not surprising that the Petition never addressed the “*n*-” in the challenged claims, or whether the prior art discloses it.

2. “consisting of”

According to Petitioner’s claim-construction position in district court, there is no disclosure in Gwozdz-PCT or Meezan meeting any of the ’786 Patent claims, because every embodiment of Gwozdz-PCT and Meezan contains some amount of water.

As detailed above (*supra* §IV), Petitioner and Dr. Donovan advocate in district court that the challenged claims exclude “water and oil.” EX2050 at 27; EX2069 (Donovan-CC Decl.) ¶¶26, 33. Accordingly, Petitioner asserts in district court that the claims exclude *even trace impurities*, such as trace amounts of water. EX2050 at 46 (emphasis added). In support of this extreme position, Dr. Donovan opined that the “consisting of” language of the ’786 Patent claims “does not allow for the inclusion of small amounts of water.” EX2069 ¶26; *see id.* ¶¶33, 50; EX2070 at 226:15-21.

Before the Board, however, Petitioner takes a completely different view. *First*, Petitioner relies on Gwozdz-PCT as disclosing solutions of diazepam in tocopherols, benzyl alcohol, and ethanol, where the ethanol indisputably contains water. Pet. at 39-40 (citing EX1062 ¶¶144-145; EX1009 at 6:16-19). At the time, it was well-known that even “dehydrated” (200-proof) ethanol is not water-free (EX1038 (USP 26) at 5) and Dr. Donovan agrees. EX2070 at 36:9-25. In the embodiment the Petition cites, Gwozdz-PCT states that “the ethanol is desirably 180 to 200 proof ethanol, *i.e.*, in the range of 90-100% ethanol.” EX1009 at 6:27-6:29. The remaining percentage of the composition (up to 10%) is almost entirely water. EX2074 ¶¶224-226.

Second, the Petition relies on an embodiment of Gwozdz-PCT discussing “penetration enhancers” as motivation to combine with Meezan. Pet. at 29, 32, 41

(citing to EX1009, subsets of 10:9-10:16). The full embodiment, however, states that pharmaceutical solutions with “penetration enhancers” are formulated “for injection by combining the instant pharmaceutical solution with, e.g., saline solution or *water*.” EX1009 at 10:6-8 (emphasis added). Whether “saline solution or *water*” is used in the formulation, water is present as an intended ingredient. EX2070 at 79:3-80:20;⁸ EX2074 ¶227.

Third, the focus of Meezan is combining therapeutic agents “with various surfactants” in aqueous solutions. EX1010 ¶[0003]; Abstract (“surfactant”). Just as every embodiment in Gwozdz-PCT includes water, every example in Meezan involves peptides or proteins dissolved in water. EX2074 ¶¶228-230. Petitioner utterly fails to address how these water-based references somehow result in the ’786 Patent inventions, which—according to Petitioner in district court—exclude every trace of water.

⁸ By extracting the “penetration enhancers” language but ignoring the remainder of the embodiment, Petitioner improperly “use[s] hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.” *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1998).

B. THERE WOULD HAVE BEEN NO REASON TO COMBINE GWOZDZ-PCT AND MEEZAN

Even if the Board were to consider motivations to combine, these too fail. Hindsight bias pervades the obviousness analysis, starting with the Petitioner's use of the '786 Patent, itself, as a basis for the motivation to combine. Petitioner takes a reference (Gwozdz-PCT) with no identified need for improvement and reworks it by adding alkyl glycosides from Meezan. And not just *any* alkyl glycoside, but the subgenus (dodecyl maltoside) containing the *one compound* the claims require, even though Meezan does not disclose it, and teaches that other alkyl glycosides would be preferable. There would have been no reason to do this, other than hindsight reconstruction, particularly since the two references are directed to different therapeutic agents and different excipients. The "proposed combination remains poorly defined and tainted by hindsight bias." *Intel Corp. v. Besang Inc.*, IPR2023-00991, Paper 40 at 36 (P.T.A.B. Dec. 26, 2024).

1. Hindsight pervades the obviousness assertion

Petitioner cites only the '786 Patent when characterizing a "known problem in the art" as "the inability to administer benzodiazepine drugs (e.g., diazepam) due to the limited solubility of the benzodiazepine drug compounds." Pet. at 27-28. Petitioner then concludes, "In view of these shortcomings, a POSA would have been motivated to improve the solubility of benzodiazepine drugs...." Pet. at 28 (emphasis added). Formulating the problem from the challenged patent itself is

improper hindsight. *See InTouch Techs., Inc. v. Vgo Commns., Inc.*, 751 F.3d 1327, 1351 (Fed. Cir. 2014) (expert improperly “relied on the [challenged] patent itself as her roadmap for putting what she referred to as pieces of a ‘jigsaw puzzle’ together”).

Petitioner asserts that “Gwozdz[-PCT] provides guidance regarding how to solubilize poorly water-soluble compounds (such as diazepam).” Pet. at 28. Identifying no deficiency in Gwozdz-PCT, Dr. Donovan asserts that “a POSA would have also looked to additional references for guidance regarding additive compositions to improve the efficacy of the pharmaceutical solutions of Gwozdz.” EX1062 ¶103. Relying on Dr. Donovan, Petitioner asserts that Gwozdz-PCT states that “additional pharmaceutically acceptable additives” can be used, Meezan has additives in it, so “a POSA was motivated to apply the teachings of Meezan related to alkyl glycosides to the pharmaceutical solutions of Gwozdz[-PCT].” Pet. at 29.

But Gwozdz-PCT does not describe any deficiencies with solubility or bioavailability or any other need for improvement once a therapeutic agent (including diazepam) is dissolved in the tocopherol and alcohol solvent system it discloses. *See* EX2070 at 58:4-14 (Gwozdz solves the problem of diazepam’s limited solubility); EX2074 ¶¶232-235, 251-252. Nor does the Petition identify any such shortcomings or reasons why Gwozdz-PCT needs modification. Petitioner has failed to demonstrate that its “[f]ormulation of the problem was derived directly from the prior art, rather than from the challenged claims.” *Purdue Pharma L.P. v.*

Depomed, Inc., 643 F. App'x 960, 966 (Fed. Cir. 2010) (rejecting obviousness assertions for improper hindsight).

Elsewhere Petitioner asserts that solubility of diazepam for intranasal applications *was already solved* in the art. Citing an Emergency Medical Services guide, Petitioner asserts that a POSA would have known that a diazepam solution could be administered intranasally in sufficient doses. Pet. at 20-21; EX1062 ¶¶76 (discussing EX1019); EX2070 at 255:4-256:1 (intranasal dose was “effective”). Dr. Donovan states that benzodiazepines had been studied and recommended for intranasal delivery, and the “medical literature is replete with examples.” EX1062 ¶¶60-61, 72-77. Thus, the very “problem” identified to motivate combining Gwozdz-PCT and Meezan was either not a problem (because it had been solved), or it was unknown in the prior art. EX2074 ¶234. Either way, there would have been no reason to combine Gwozdz-PCT and Meezan, absent hindsight.

2. The Petition does not identify any reason to modify Gwozdz-PCT

Even if one pretends that the Petition derived the “known problem” of limited solubility of diazepam from the prior art, rather than the '786 Patent (Pet. at 27), Gwozdz-PCT states that it solves the problem. There would have been no need or reason to modify Gwozdz-PCT with additional excipients from Meezan.

Gwozdz-PCT states that its formulation was successful, without any identified deficiencies. Gwozdz-PCT states that its formulation is “less irritating to the skin and/or mucous membranes,” “provides a higher loading of therapeutic agent,” and “provides for improved ability to dissolve hydrophilic and lipophilic therapeutic agents,” such as diazepam. EX1009, 5:4-5:7, 9:19-10:2. Gwozdz-PCT does not identify any need for improvement. EX2074 ¶¶237-238.

Petitioner asserts that “while Gwozdz was focused on pharmaceutical solutions developed to improve the solubility of drugs with solubility issues,” Meezan presented a distinct approach of utilizing compounds that increase the absorption and bioavailability of drug compounds. Pet. at 29. This is pure hindsight, because Gwozdz-PCT states that it already succeeded in “providing increased bioavailability of the therapeutic agent.” EX1009, 7:5-8; *see* 4:34-5:2, 5:30-31, 8:30-31. Furthermore, Petitioner contends that, once diazepam was made sufficiently soluble (as in Gwozdz-PCT), improved bioavailability inherently followed: “It was well-known that benzodiazepines have sufficient lipophilic character to readily cross biologic membranes [citing EX1027].” Pet. at 19; EX1062 ¶65. Thus, absent hindsight, a POSA would not have considered Meezan to improve Gwozdz-PCT. EX2074 ¶¶238-244.

In summary, even if a POSA *could* have modified the formulation of Gwozdz-PCT, that does not mean the POSA *would* have done so. *See Virtek Vision Int’l ULC*

v. Assembly Guidance Sys., Inc., 97 F.4th 882, 886-87 (Fed. Cir. 2024) (“[O]bviousness concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of prior art to arrive at the claimed invention.”); *Adidas AG v. Nike, Inc.*, 963 F.3d 1355, 1359 (Fed. Cir. 2020) (similar quote re “would have been motivated”). The Petition fails to prove that a POSA would have been motivated to make the identified modifications that are predicates to obviousness.

3. Interactions with other excipients

Before making the modification Petitioner proposes to Gwozdz-PCT, there would need to be a reason for doing so. EX2074 ¶245. Petitioner supplies no such reason, and its analysis on motivations to combine “should be made explicit.” *See KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). The Petition does not even cite to *KSR*, let alone provide any of the exemplary rationales to support obviousness. *See* M.P.E.P. §2143(I) (“Examples of Rationales under *KSR*”).

a. Ethanol and benzyl alcohol

The specific alcohols recited in the claims provide additional reasons that, absent hindsight, a POSITA would not have modified the formulation of Gwozdz-PCT to include Meezan:

1. A pharmaceutical solution for nasal administration consisting of:
a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof;
one or more natural or synthetic tocopherols or tocotrienols selected from the group consisting of α -tocopherol, β -tocopherol, γ -tocopherol, δ -tocopherol, α -tocotrienol, β -tocotrienol, γ -tocotrienol, δ -tocotrienol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w);
one or more alcohols in an amount from 10% to 70% (w/w), wherein the one or more alcohols comprises benzyl alcohol; and
n-dodecyl beta-D-maltoside.

11. A pharmaceutical solution for nasal administration consisting of:
a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof;
one or more natural or synthetic α -tocopherols selected from the group consisting of tocopherol, β -tocopherol, γ -tocopherol, δ -tocopherol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w);
one of more alcohols in an amount from 10% to 70% (w/w), wherein the one or more alcohols comprises benzyl alcohol; and
n-dodecyl beta-D-maltoside.

Petitioner asserts that a POSA would have been motivated to include benzyl alcohol in the formulation of Gwozdz-PCT, because “a POSA would also know that benzyl alcohol provides other advantageous properties to the formulation, including its function as an antimicrobial preservative.” Pet. at 34 (citing EX1016 at 9). Yet the monograph Petitioner cites states that the “antimicrobial activity [of benzyl alcohol] is reduced in the presence of nonionic surfactants,” and “Ethanol is inactivated in the presence of nonionic surfactants.” EX1016 at 10, 14; *see* EX1001, claims 7, 17 (reciting “ethanol”). Thus, Petitioner’s proposed modification of Gwozdz-PCT by including one excipient (*n*-dodecyl- β -D-maltoside, a non-ionic surfactant) would deactivate other excipients. EX2074 ¶253; *see Medtronic, Inc. v. Teleflex Innovations S.a.r.l.*, 69 F.4th 1341, 1349-1350 (avoiding “hindsight bias” by considering whether “a proposed modification would interfere with a reference’s stated purpose”).

The same monograph on which Dr. Donovan relies also explains that ethanol is a “skin penetrant,” which is synonymous with a penetration enhancer. EX1016 at 13; EX2070, 169:21-170:4. A POSA would not have been motivated to add *any* absorption enhancer to the formulation of Gwozdz-PCT, let alone a second one. EX2074 ¶254.

b. Tocopherols/tocotrienols

Claims 1 and 11 each recite tocopherols/tocotrienols:

1. A pharmaceutical solution for nasal administration consisting of:
a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof;
one or more natural or synthetic tocopherols or tocotrienols selected from the group consisting of α -tocopherol, β -tocopherol, γ -tocopherol, δ -tocopherol, α -tocotrienol, β -tocotrienol, γ -tocotrienol, δ -tocotrienol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w);
one or more alcohols in an amount from 10% to 70% (w/w), wherein the one or more alcohols comprises benzyl alcohol; and
n-dodecyl beta-D-maltoside.

11. A pharmaceutical solution for nasal administration consisting of:
a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof;
one or more natural or synthetic α -tocopherols selected from the group consisting of tocopherol, β -tocopherol, γ -tocopherol, δ -tocopherol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w);
one of more alcohols in an amount from 10% to 70% (w/w), wherein the one or more alcohols comprises benzyl alcohol; and
n-dodecyl beta-D-maltoside.

These compounds were known to be unstable generally and sensitive to degradation from exposure to light, heat, oxygen, and water, leading to discoloration over time. *See* EX2070 at 283:18-284:13. A POSA would have been particularly cautious in modifying a working formulation containing tocopherols/tocotrienols, as in Gwozdz-PCT. EX2074 ¶¶82-88, 264-268 (citing EX2053-EX2059).

4. The “other pharmaceutically acceptable additives” embodiment does not establish motivation to combine

Petitioner relies on a passage in Gwozdz-PCT that formulations may include a long list of “additional pharmaceutically acceptable additives,” including “penetration enhancers.” Pet. at 29 (citing EX1009 at 10:12-16). Petitioner then asserts that Meezan discloses “absorption enhancers” and that “[b]ased on this, a POSA was motivated to apply the teachings of Meezan related to alkyl glycosides to the pharmaceutical solutions of Gwozdz.” *Id.* As described above, just because a POSA *could* add something to Gwozdz-PCT does not mean that the POSA *would* have. There are several additional flaws with Petitioner’s approach.

a. The “penetration enhancer” language in Gwozdz-PCT was added in 2009

The “penetration enhancers” does not appear in Gwozdz-Provisional (EX1064). Rather, its first appearance is in 2009 in Gwozdz-PCT itself. *See supra* §VII.B; EX2074 ¶247. The “penetration enhancers” is unavailable as prior art. *See Riggs*, 131 F.4th at 1384 (“portion of the application relied on ... as prior art must be supported by the provisional application”).

b. The “other pharmaceutically acceptable additives” embodiment conflicts with other claim limitations and is not for intranasal applications

To the extent the “penetration enhancer” language is even considered (and it should not be, because it is not prior art), Petitioner also ignores the context of the

“other pharmaceutically acceptable additives” embodiment of Gwozdz-PCT in which the phrase “penetration enhancers” is found.

First, Petitioner asserted that the challenged claims should be construed to exclude all water, even trace impurities. *See supra* §§IV, IX.A.2. Yet, “other pharmaceutically acceptable additives” embodiment specifically includes added saline or water. EX1009, 10:3-10:14; EX2074 ¶¶248-249. The disclosure in this embodiment would, if anything, have led a POSA to develop injectable aqueous/saline compositions—not the claimed intranasal, non-aqueous compositions.

Second, the broader context of Gwozdz-PCT demonstrates that “other pharmaceutically acceptable additives” are not for nasal applications. Gwozdz-PCT provides an introduction with a laundry list of applications, concluding that the “most suitable route in any given case will depend on the nature and severity of the condition being treated and on the nature of the particular therapeutic agent which is being used.” EX1009, 8:32-9:18. Gwozdz-PCT then describes embodiments: nasal (*id.*, 9:20-10:2); injections (10:3-10:16); oral (10:17-11:16); parenteral (11:17-26); topical (11:27-12:27); and transdermal applications (12:28-13:3). The reference to “other pharmaceutically acceptable additives” appears in the embodiment on injection application (10:3-10:16), but not in the section for “nasal applications.” *See* EX2070 at 87:15-21; EX2074 ¶249. For motivation to combine, Petitioner

extracts an “other pharmaceutically acceptable additive” from an injected formulation and, absent any reasoning or explanation, applies it to a nasal formulation. That maneuver requires impermissible hindsight.

5. Even if a POSA were to modify Gwozdz-PCT, there is no reason to modify with Meezan

Meezan does not mention “diazepam” or “benzodiazepine” or disclose their use. EX2070 at 148:25-149:10. Nor does Meezan mention or disclose applications of tocopherols. *Id.*, 150:1-150:7. A POSA would have recognized, based on these missing limitations and others, that Meezan and Gwozdz-PCT are directed to different applications and would not have combined the references in the way Petitioner does. EX2074 ¶¶255-258. *See Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1332 (Fed. Cir. 2019) (“the prior art must be considered for all its teachings, not selectively”).

a. Meezan is directed to large macromolecules, not smaller molecules like benzodiazepines

To the extent a POSA would have considered modifying Gwozdz-PCT (for which there is no motivation), the POSA would not have looked to Meezan.

Meezan does not address benzodiazepines or diazepam because Meezan concerns itself with stabilizing solutions and increasing bioavailability of peptides, proteins, nucleic acids, and other such macromolecules. EX1010 ¶¶[0064], [0070], [0092], [0146]-[0172] (Examples 1-7). These molecules are many thousands of

Daltons (e.g., 30,000 Daltons), while diazepam is a typical “small molecule” with a molecular weight of only 285 Daltons. EX2074 ¶¶259-260.

While Meezan says it “anticipate[s]” using the disclosed methods with “small” molecules, that would have informed a POSA that such an application was simply a hypothesis—not a known application or actual teaching. EX1010 ¶[0130]. Indeed, every example in Meezan formulates peptides or proteins, not small molecules. EX2070 at 141:9-142:1, 143:14-18. And even considering the “small molecules,” for which Meezan provides no examples, they are significantly larger than the 285 Daltons of diazepam. This observation also correlates with the disclosed sizes for what Meezan considers “small molecules”: “an organic compound that has a molecular weight of less than 3 kD, or less than 1.5 kD.” EX1010 ¶[0130]. Meezan also refers to compounds that are “low molecular weight,” but Meezan defines the range very broadly to include molecules of 1,000-30,000 Daltons (“1-30 kiloDaltons”). EX1010 ¶¶[0012]-[0013]; *see* EX1010 ¶¶[0004], [0076], [0089], [0099], [00132], [0136]. This range includes peptides, proteins, and other biologics having molecular weights that are orders of magnitude larger than diazepam. EX2074 ¶260.

Petitioner handwaves the differences between what Meezan teaches (macromolecules) and what Gwozdz-PCT teaches (diazepam) by asserting:

Larger molecules inherently have a more difficult time crossing the cell

membrane compared to smaller molecules.... [I]f a compound is shown to increase penetration and absorption for a large molecule, it will be expected to also increase penetration and absorption for a small molecule.

Pet. at 32-33. This argument can only make sense from a hindsight perspective. By corollary, a small molecule (e.g., diazepam in Gwozdz-PCT) does not have as much difficulty passing through the cell membrane as a large molecule. Thus, while an absorption enhancer may have been needed for the macromolecules in Meezan, a POSA would have considered an enhancer superfluous—and would not have used it—for the small molecules in Gwozdz-PCT, such as diazepam. EX2074 ¶261; *see In re Anova Hearing Labs, Inc.*, 809 F. App'x 840, 843 (Fed. Cir. 2020) (nonprecedential) (rejecting motivation to combine where primary reference already addressed the issue the “Board does not explain why a person of skill in the art would conclude that [the primary reference] needed to be modified”); *Ex Parte Tsai-Ching Lu, et al.*, Appeal 2022-000521, 2022 WL 4957922, at *3 (P.T.A.B. Sept. 30, 2022) (“Adding a redundant feature does not constitute a reason to combine.”).

b. Meezan does not teach compatibility with tocopherol or tocopherol/alcohol carriers

Meezan also fails to teach application to tocopherol-based solutions. Petitioner relies on Meezan ¶[0074] to state that “alkyl glycosides were shown to be successfully utilized in non-aqueous solvent systems.” Pet. at 33. This is

Petitioner's only support for using the disclosure of Meezan with a non-aqueous system. Petitioner misreads the passage. EX2074 ¶262.

First, even Dr. Donovan does not contend that Meezan discloses using alkyl glycosides with tocopherol-containing solutions like those of Gwozdz-PCT. Nowhere does "tocopherol," "tocotrienol," "vitamin E," or any analog. EX2070 at 149:7-150:7; EX2074 ¶263.

Second, every disclosed Example in Meezan adds alkyl glycosides to aqueous solutions of peptides or proteins. None of the Examples applies alkyl glycosides to any form of nonaqueous solution (let alone diazepam or any other small molecule). The presence of water in the solutions of Meezan provides another reason to not combine Meezan with Gwozdz-PCT to arrive at the claimed invention. The claimed invention requires tocopherols, and it was known that tocopherols are susceptible to degradation in water. EX2074 ¶¶264-265; *see supra* §IX.B.3.b. In this way, Gwozdz-PCT (tocopherol solution) and Meezan (aqueous solution of alkyl glycosides) are incompatible. *See Adidas*, 963 F.3d at 1358-59 (no motivation to combine where doing so would change a reference's operating principles or render it inoperable for its intended purpose).

C. EVEN IF GWOZDZ-PCT AND MEEZAN WERE COMBINED, A POSA WOULD NOT HAVE ARRIVED AT THE CLAIMED INVENTION

Even if a POSA would have considered Meezan, there would have been no reason to modify Gwozdz-PCT to add dodecyl maltoside, let alone *n*-dodecyl- β -D-maltoside (which Meezan does not disclose). To the contrary, Meezan would have directed a POSA towards branched (non-linear) alkyl glycosides, which does not result in the claimed inventions. EX2074 ¶269.

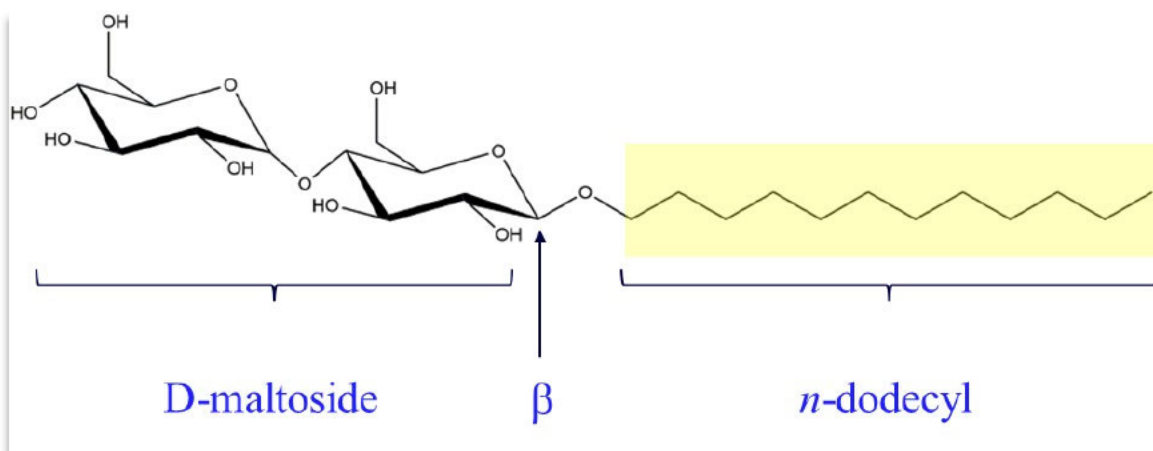
The Petition cites no evidence, as there is none, for any disclosure of “*n*-dodecyl β -D-maltoside” in Gwozdz-PCT or Meezan. EX2074 ¶¶270-271. Rather, the Petition asserts “a POSA would routinely select dodecyl maltoside to add to Gwozdz’s solution.” Pet. at 41 (citing EX1062 ¶151). First, “dodecyl maltoside” is a subgenus (of alkyl glycosides), not the claimed species, and nothing in Gwozdz-PCT or Meezan teaches using the linear (“*n*-”) isomer of dodecyl maltoside. Second, neither Petitioner nor Dr. Donovan provides any citations to Gwozdz-PCT or Meezan—or any other evidence—to support that a POSA would “routinely select” dodecyl maltoside. Nor do they provide any *KSR* rationales or other reasoning to support this conclusory assertion. *See GCE Control Equipment Inc. v. VBOX Inc.*, IPR 2023-00326, Paper 27 at 53 (P.T.A.B. June 18, 2024) (“Under the particular facts at hand, we detect the unmistakable taint of impermissible hindsight reconstruction in Petitioner’s conclusory proposition.”).

1. Meezan's disclosure of isomeric structure

The only location where Meezan describes the isomeric structure of dodecyl maltoside would direct a POSITA *away from* the claimed linear species. Meezan states:

Stability of the alkyl glycoside depends, in part, on the number of carbon atoms, or branching of the alkyl chain, with tetradecylmaltoside (TDM) having the greatest effect; but other ***highly branched alkyl chains including DDM*** [dodecyl maltoside] also have stabilizing effects.

EX1010 ¶[0149] (emphasis added); EX2074 ¶¶272-273. In this passage Meezan leads a POSA to conclude that if dodecyl maltoside is used, the isomer to choose is one with “branching” or even “highly branched” isomers. Among the 355 isomers of dodecyl-beta-D-maltoside, Meezan teaches that the subgenus includes the branched isomers, but not the claimed “*n*-dodecyl-beta-D-maltoside.” The species recited in the '786 Patent claims is linear, not branched. *See supra* §VI.



EX2074 ¶¶69-72, 81.

2. Importance of “highly branched” and longer chains

Meezan discloses the importance of how “an ideal enhancing surfactant will stabilize the therapeutic agent” and, to achieve this goal, Meezan recommends using “highly branched” glycosides. EX1010 ¶¶[0003], [0149]. As a matter of basic organic chemistry, the longer the carbon chain, the more branching that can occur. EX2070, 24:15-25:12. Accordingly, Meezan discloses that tetradecyl maltoside (“TDM,” having a 14-carbon alkyl chain) has “the greatest effect,” not dodecyl maltoside (12-carbon alkyl chain). EX1010 ¶[0149]. According to Meezan, the longer the alkyl chain, the more effective the absorption enhancer. EX1010 ¶[0157]. The “alkyl chain length, as well as the carbohydrate moiety,” has a “critical” role. EX1010 ¶[0160]. Thus, Meezan teaches to use a longer, more branched chain: TDM exceeds DDM, and “highly branched” alkyl groups have the greatest effect. Yet the claimed species is linear (not branched) DDM (not TDM). EX2074 ¶¶274-277.

3. Examples 1-7 of Meezan would lead a POSA to TDM, not *n*-dodecyl- β -D-maltoside

Meezan includes some data, presented in seven numbered Examples, analyzing certain qualities of several alkyl glycosides. EX1010 ¶¶[0146]-[0172]. The POSA would have made several observations from these disclosures.

First, every example incorporates an alkyl glycoside with a peptide or a protein, rather than a small molecule like diazepam. This choice would have made

sense to a POSA in 2008-2009, as it was known that large molecules like peptides, proteins, and nucleic acids are poorly absorbed when administered by extravascular routes. EX1062 ¶¶110-112. This evidence would not have led the POSA to apply Meezan to a small molecule application, such as the diazepam solutions of Gwozdz-PCT, for which there was no need of it. EX2074 ¶¶278-280.

Second, every Example in Meezan examines characteristics of TDM. EX1010 ¶¶[0146]-[0172]. As discussed below, TDM (and other alkyl glycosides) work better than dodecyl maltoside in Meezan. Among the options, Meezan's data show that dodecyl maltoside was the least effective alkyl glycoside and, in certain tests, totally ineffective. Thus, to the extent a POSA would have even looked to Meezan for an absorption enhancer for Gwozdz-PCT, the POSA would have been led to use TDM and not dodecyl maltoside, and certainly not the linear isomer (*n*-dodecyl- β -D-maltoside). See EX2070 at 121:7-11 (Meezan disclosing that TDM has "the greatest effect"); EX2074 ¶¶280-285.

4. Meezan expresses no suggestion of *n*-dodecyl- β -D-maltoside

Meezan provides a "Summary of the Invention" stating that "the present invention" includes "enhancing agents" that include "an alkyl glycoside and/or saccharide alkyl ester." EX1010 ¶[0004]. These categories of compounds are so generic as to encompass countless potential molecules. A POSA would not have

understood Meezan to disclose that *n*-dodecyl- β -D-maltoside is a preferred alkyl glycoside (or even disclosed at all). EX2074 ¶¶286-287.

The vastness of “alkyl glycoside and/or saccharide alkyl ester” results from the modular nature of these types of compounds, the many options for those moieties, and the various permutations resulting from varying one or more of those moieties. The variables characterizing these categories of compounds at least include: (i) the saccharide or glycoside (e.g., which sugar); (ii) the stereochemistry of the saccharide or glycoside (e.g., D or L); (iii) the anomeric structure of the saccharide or glycoside (α or β); (iv) substitution of heteroatoms (e.g., sulfur); (v) the alkyl chain (its size and its isomeric structure); and (vi) the linking chemistry between the moieties. EX2074 ¶¶79, 288-296.

Meezan discloses alkyl groups from 8 to 24 carbon atoms. EX1010 ¶¶[0056], [0058]; EX2074 ¶289. Regarding isomerization, the only structural isomers even mentioned are “highly branched” (not linear). EX1010 ¶[0149]; EX2074 ¶290. Meezan lists many options as potential glycosides (the sugar moiety). EX1010 ¶[0058]; EX2074 ¶291. Meezan expresses a preference for heteroatom substitution (i.e., replacing a carbon atom with a non-carbon and non-hydrogen), rather than an unsubstituted glycoside. EX1010 ¶¶[0056], [0075]; EX2074 ¶292. Meezan discloses numerous types of linkages between the alkyl group and the glycoside, and both anomeric configurations. EX1010 ¶¶[0002], [0056], [0061], [0075]; EX2074

¶¶293-294. The only reasonably particular preference Meezan discloses is for TDM (14 carbons, not dodecyl maltoside): “An even more preferred range is from about 9 to about 16 *or about 14 carbon atoms.*” EX1010 ¶[0058] (emphasis added). And even for this option, Meezan elsewhere discloses TDM as “highly branched,” rather than having a linear alkyl chain. EX1010 ¶[0149]; EX2074 ¶¶295-296; *see Kuban*, 561 F.3d at 1359 (“where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness”).

Petitioner’s assertion that a POSA would naturally choose one particular compound (*n*-dodecyl- β -D-maltoside, which is not even disclosed and which Meezan teaches against) is unsupported. EX2074 ¶¶297-300. Thus, what Petitioner states about the ’558 Provisional—that it does not identify “whether any of the alkyl glycosides are useful or preferred over any of the other hundreds of ... candidates disclosed” (Pet. at 16)—more appropriately applies to Meezan. Whereas the ’558 Provisional discloses *n*-dodecyl- β -D-maltoside verbatim, Meezan does not disclose it at all, and instead teaches using a “highly branched” compound.

X. GROUND 2: CARTT-784

Cartt-786 and the ’786 Patent “were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.” *See* 35 U.S.C. §103(c)(1). Specifically, Cartt-784 and the ’784 Patent

(and parent applications) were owned by and assigned to Questcor or its successors in interest. Accordingly, Cartt-784 cannot serve as the basis for an obviousness challenge under §103(c)(1). Even assuming Cartt-784 were not excluded under §103(c)(1), it would still be unavailable under §103(c)(2) for the same reasons discussed above with respect to Gwozdz-PCT in view of the JRA.

To the extent Cartt-784 (EX1065) can even be used in an obvious combination (it cannot), there would have been no motivation, absent hindsight, to combine with Gwozdz-PCT and Meezan. Petitioner's only argument for motivation to combine is that all three references are "directed to benzodiazepine nasal formulations." Pet. at 62. This does not suffice.

First, as described above, Meezan does not even mention benzodiazepine, and it is certainly not "directed to" benzodiazepine formulations. Rather, Meezan is directed to proteins and other macromolecules. EX2074 ¶¶301-304.

Second, after spending "eleven minutes" at deposition to review Cartt-784 to "refresh [her] memory" about it, Dr. Donovan admitted that "all of the examples contained particles containing an active pharmaceutical ingredient." EX2070 at 176:11-177:24. For example, Cartt-784 is directed to "[p]articulate formulations of benzodiazepines," which are used in a "suspension." EX1065 at Abstract, ¶¶[0015], [0017] [0021]-[0023]. As Dr. Brown explains, a suspension is a heterogenous mixture of two substances, in which solid particles are "suspended" within a liquid

phase. In contrast, a solution (as in Meezan) mixes two or more substances homogenously with each other. EX2074 ¶¶95-103. These two routes have different characteristics. EX2074 ¶¶305-306.

XI. GROUND 3: USP23/NF18

Petitioner provides no discussion or support for its assertion that USP23/NF18 (EX1066) “published in 1995” and is §102(b) prior art. Pet. at 25. “[T]here is no presumption ... in favor of finding a reference to be a printed publication” *See Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29 at 16 (P.T.A.B. Dec. 20, 2019) (precedential). Here, Petitioner provides no “supporting declaration” or any other evidence that the USP23/NF18 was “indexed, cataloged, and shelved” in any library or database, or that the USP23/NF18 “has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it.” *Id.* at 9, 11, 15; *see Medivis, Inc. v. Novarad Corp.*, IPR2023-00042, Paper 35 at 27 (P.T.A.B. Mar. 26, 2024) (“Numerous Board decisions have held that simply pointing to a date, even a copyright date, is not sufficient at the institution stage to demonstrate public accessibility” and is “even more inadequate” post-institution).

XII. COLLATERAL ESTOPPEL DOES NOT APPLY

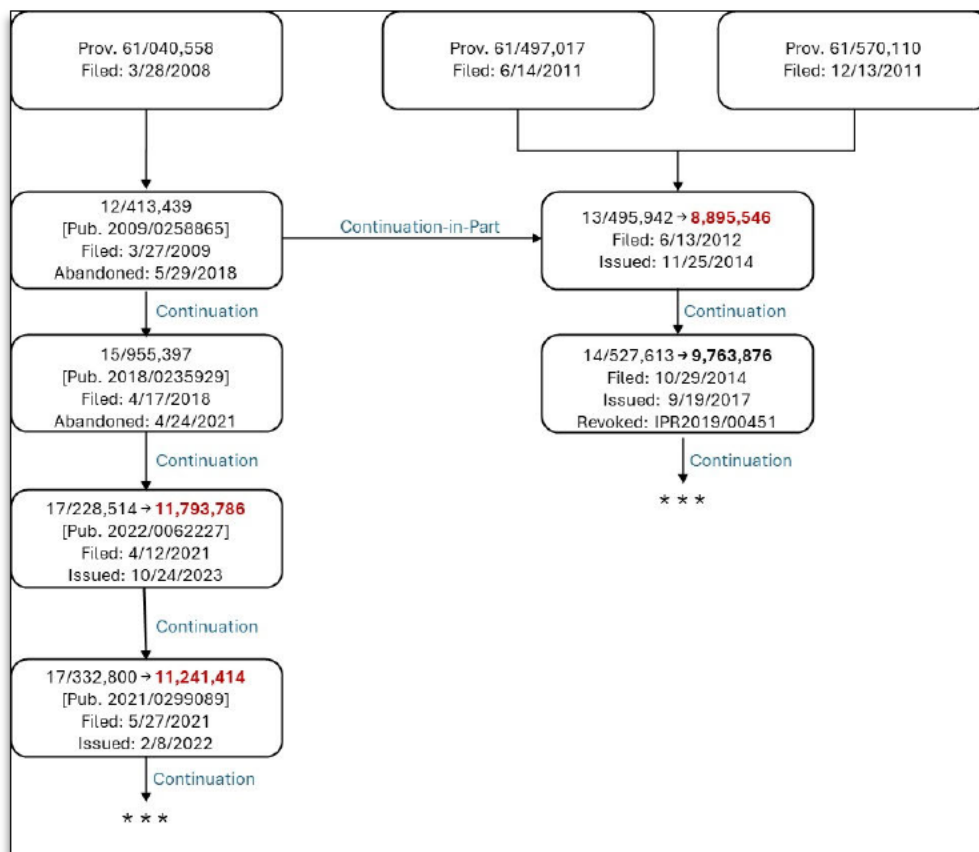
As the “party seeking to invoke collateral estoppel,” Petitioner “must show” four elements:

(1) the issue is identical to one decided in the first action; (2) the issue was actually litigated in the first action; (3) resolution of the issue was essential to a final judgment in the first action; and (4) the party against whom collateral estoppel is being asserted had a full and fair opportunity to litigate the issue in the first action.

Google v. Hammond Development Int’l, Inc., 54 F.4th 1377, 1381 (Fed. Cir. 2022).

Additionally, collateral estoppel “does not apply where ‘a new determination is warranted in order to take account of an intervening change in the applicable legal context or otherwise to avoid inequitable administration of the laws.’” *Dow Chem. Co. v. Nova Chems. Corp. (Canada)*, 803 F.3d 620, 628 (Fed. Cir. 2015) (quoting Restatement (Second) of Judgments §28(2) (1982)).

As is undisputed, the ’786 Patent was never actually litigated. Only the ’876 Patent, from a different branch on the family tree, was litigated.



EX2068. “[S]eparate patents describe separate and distinct inventions, and it cannot be presumed that related patents rise and fall together.” *Comair Rotron, Inc. v. Nippon Densan Corp.*, 49 F.3d 1535, 1539 (Fed. Cir. 1995) (internal citations omitted) (reversing finding of collateral estoppel).

Petitioner’s attempts to shoehorn the 451 IPR into the ’786 Patent also fail because the ’786 Patent’s priority issues are materially different and were never actually litigated, the Gwozdz-PCT priority issues were not litigated and are subject to an intervening change in law, and the ’786 Patent’s claim limitation requiring *n*-

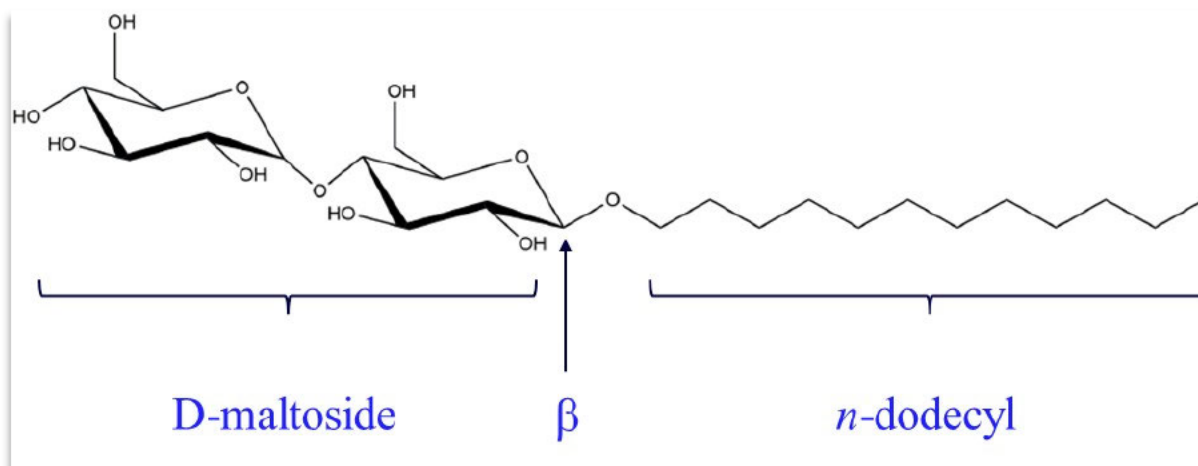
dodecyl- β -D-maltoside was not present in the '876 Patent, leading to importantly-differing analyses, including of motivation to combine.

A. PETITIONER FAILS TO SHOW THAT COLLATERAL ESTOPPEL APPLIES TO PRIORITY DATE

As the Board held, “Petitioner does not persuade us that collateral estoppel applies to the priority issue raised here. Invocation of collateral estoppel would require identity between the priority issues in this proceeding and in the 451 IPR.” Paper 13 at 23; *see ParkerVision, Inc. v. Qualcomm Inc.*, 116 F.4th 1345, 1356 (Fed. Cir. 2024) (does not apply when claims are “materially different” from those previously litigated). Although the *claims* between the two patents need not be identical (and indeed are not), collateral estoppel still “requires that the *issues of patentability* be identical.” *Google*, 54 F.4th at 1381 (citing *Ohio Willow Wood Co. v. Alps South, LLC*, 735 F.3d 1333, 1342 (Fed. Cir. 2013)); *see MaxLinear, Inc. v. CF CRESPE LLC*, 880 F.3d 1373, 1377-78 (Fed. Cir. 2018) (remanding where Board applied collateral estoppel to independent claims but failed to separately analyze dependent claims).

First, the '876 and '786 Patents are directed to different statutory classes. *See* 35 U.S.C. §101. The '876 Patent claims recite “[a] method of treating a patient,” whereas the '786 Patent claims recite “[a] pharmaceutical solution.”

Second, the '876 and '786 Patents claim different subject matter. Every claim of the '786 Patent specifically requires *n*-dodecyl- β -D-maltoside, a chemical compound with a specific chemical structure:



In contrast, the '876 Patent claims recite a broad subgenus of “dodecyl maltoside” (claim 26) and an even broader genus of “alkyl glycoside” (claim 1); EX2074 ¶¶196-197. This can be seen from Petitioner’s claim-chart comparison (gray items):

<u>Claims 1, 4, 7 and 26 of 9,763,876 Found Unpatentable in IPR 2019-00451</u>	<u>Claim 1 of 11,793,786</u>
1. A method of treating a patient with a disorder which is treatable with a benzodiazepine drug, comprising: administering to one or more nasal mucosal membranes of a patient a pharmaceutical solution for nasal administration consisting of a benzodiazepine drug, one or more natural or synthetic tocopherols or tocotrienols, or any combinations thereof, in an amount from about 30% to about 95% (w/w); ethanol and benzyl alcohol in a combined amount from about 10% to about 70% (w/w); and an alkyl glycoside. 4. The method of claim 3, wherein the benzodiazepine drug is diazepam, or a pharmaceutically-acceptable salt thereof. 7. The method of claim 1, wherein the one or more natural or synthetic tocopherols or tocotrienols are selected from the group consisting of: α-tocopherol, β-tocopherol, γ-tocopherol, δ-tocopherol, α-tocotrienol, β-tocotrienol, γ-tocotrienol, δ-tocotrienol, tocophersolan, any isomers thereof, any esters thereof, any analogs or derivatives thereof, and any combinations thereof. 26. The method of claim 25, wherein the solution contains about 0.01% to 1% (w/w) of dodecyl maltoside.	1. A pharmaceutical solution for nasal administration consisting of: a therapeutically effective amount of diazepam or a pharmaceutically acceptable salt thereof; one or more natural or synthetic tocopherols or tocotrienols selected from the group consisting of α-tocopherol, β-tocopherol, γ-tocopherol, δ-tocopherol, α-tocotrienol, β-tocotrienol, γ-tocotrienol, δ-tocotrienol, tocophersolan, any isomers thereof, any esters thereof, and any combinations thereof, in an amount from 30% to 95% (w/w); one or more alcohols in an amount from 10% to 70% (w/w), wherein the one or more alcohols comprises benzyl alcohol; and n-dodecyl beta-D-maltoside

Pet. at 2. Every '786 Patent claim requires "*n*-dodecyl beta-D-maltoside," not "dodecyl maltoside" or "alkyl glycoside." As the Board explained, "Whether a species is described adequately under 35 U.S.C. §112 versus whether a class/genera inclusive of the species is described are not identical inquiries." Paper 13 at 24. The 451 IPR had no need to address (and did not address) whether the '558 Provisional

provides sufficient written description for the particular compound, *n*-dodecyl- β -D-maltoside. *Cf.* EX2076. This makes the issues entirely non-overlapping, particularly when written description analysis is highly fact specific. *See Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1377 (Fed. Cir. 2017) (“[E]ach case involving the issue of written description must be decided on its own facts.”) (alterations and quotations omitted).

The category of alkyl glycosides encompasses vast classes of structurally distinct molecules varying in characteristics such as chain length (number of carbons), isomeric configuration (e.g., linear versus branched, as well as the degree of branching), stereochemistry, and linkage chemistry. EX2074 ¶¶79, 199, 288. These structural differences are not academic; they alter functional and biologic properties. EX2070 at 22:10-23:22, 25:13-25:24; EX2074 ¶201. And, as discussed above, Meezan does not teach *n*-dodecyl- β -D-maltoside, instead favoring “highly branched” (i.e., non-linear) alternatives. The ’786 Patent claims would not have been obvious over the ’876 Patent claims. EX2074 ¶202.

Petitioner’s collateral estoppel argument should be rejected for what it is: an attempt to evade its burden to prove invalidity of each challenged claim on a claim-by-claim basis—a showing it cannot make. Petitioner has not even attempted to establish identity of issues for each claim. *See MaxLinear*, 880 F.3d at 1377-78.

Third, collateral estoppel fails because it applies only to issues “actually litigated,” not issues that merely “*could have been raised* in the prior litigation.” *Purdue Pharma L.P. v. Iancu*, 767 F. App’x 918, 922-23 (Fed. Cir. 2019) (cleaned up) (original emphasis). As discussed above, every ’786 Patent claim requires *n*-dodecyl- β -D-maltoside. In contrast, the 451 IPR addressed patentability of claims broadly covering “an alkyl glycoside” genus:

Claim 1 requires “an alkyl glycoside.” Ex. 1001, 63:34. Since all of the remaining claims of the ’876 patent depend, directly or indirectly, from Claim 1, they also require the presence of “an alkyl glycoside.”

EX1040, 14 n.6; *see* 19 n.7 (discussing “the ‘alkyl glycoside’ limitation in the claims”), 23 (“’558 provisional does not provide adequate written description support for the ‘alkyl glycoside’ limitation. Therefore, the claims of the ’876 patent are not entitled to the benefit of priority to the ’558 provisional.”).

Fourth, Petitioner has not shown the parties in the 451 IPR actually litigated written description support in the ’558 Provisional for the dependent claims in the ’876 Patent reciting the subgenus “dodecyl maltoside” (and certainly not the *n*-dodecyl- β -D-maltoside species of the ’786 Patent claims). To the contrary:

- 1) The patent owner’s only suggestion of adequate written description for claims involving dodecyl maltoside “appears to have been relegated to a footnote”;
- 2) It was unclear whether the Board deemed this issue waived; and
- 3) The Board’s decision addressed only the “alkyl glycoside” limitation.

Paper 13 at 25-26. In short, Petitioner cannot establish that these issues were actually litigated (Factor 2), and collateral estoppel fails. The 451 IPR petitioner itself recognized that the Board did not squarely address the “dodecyl maltoside” piece, arguing to the Federal Circuit that “Neurelis waived any argument that the listing of dodecyl maltoside in the SIGMA catalog provides adequate written description support.” EX2028, 64. A predicate of this argument was failure of the parties to join battle on—or the Board to make specific findings concerning—whether the ’558 Provisional supported “dodecyl maltoside.” Thus, Factor 3 of collateral estoppel also is not met.

B. PETITIONER FAILS TO SHOW THAT COLLATERAL ESTOPPEL APPLIES TO THE PRIORITY DATE OF GWOZDZ-PCT

Collateral estoppel does not apply to Gwozdz-PCT’s prior art status in this case. “Patent Owner’s apparent concession that Gwozdz [PCT] was prior art during the 451 IPR does not equate to the issue being actually litigated.” Paper 13 at 35 n.20. Indeed, the final written decision in the 451 IPR noted: “Patent Owner does not contest that Gwozdz [PCT] is entitled to this filing date” of Gwozdz-Provisional. EX1040, 14. Failure to contest an issue, or even stipulating to an issue, does not comprise litigating that issue for collateral estoppel purposes. *See Purdue Pharma*, 767 F. App’x. at 922 (“An issue is not actually litigated ... if it is a stipulation

between the parties.... [or] a judgment entered by confession, consent, or default....”).

The 451 IPR panel found Gwozdz-PCT was entitled to the benefit of Gwozdz-Provisional, but only because the PCT claims were identical to the provisional claims. EX1040 at 13-14. The Board relied on then-controlling Federal Circuit precedent, which allowed a reference patent to trace priority to its provisional application if the provisional merely provided written-description support for the reference patent’s claims. *Id.* at 14 (citing *Dynamic Drinkware, LLC v. National Graphics, Inc.*, 800 F.3d 1375, 1381 (Fed. Cir. 2015)).

Last year, however, the Federal Circuit tightened the requirements for a prior art reference to trace priority to a provisional. In addition to supporting a claim, a “provisional application *must also* provide written description support for the specific portions of the patent specification identified and relied on in the prior art rejection.” *Riggs*, 131 F.4th at 1384 (emphasis added). A reference constitutes prior art only for what “it teaches as of its earliest accorded filing date.” *Id.* at 1385.

Here, Petitioner relies on Gwozdz-PCT’s use of “penetration enhancer” to establish a motivation to combine. But that term appears nowhere in Gwozdz-Provisional. *See supra* §VII.B. Thus, under *Riggs*, Petitioner cannot rely on the “penetration enhancer” disclosure of Gwozdz-PCT and cannot establish priority to Gwozdz ’281 provisional. The 451 IPR decision was based on a different set of facts

and law, and collateral estoppel does not apply. *Dow Chem.*, 803 F.3d at 629-30; *see Bingaman v. Dep't of Treasury*, 127 F.3d 1431, 1437-38 (Fed. Cir. 1997) (finding collateral estoppel inapplicable where later agency decisions adopted “significantly narrower” interpretation of statutory standard than did administrative judge in prior case).

C. PETITIONER FAILS TO SHOW THAT COLLATERAL ESTOPPEL APPLIES TO OBVIOUSNESS OVER GWOZDZ-PCT/MEEZAN OR OVER GWOZDZ-PCT/MEEZAN/CARTT-784

Collateral estoppel does not apply to whether there existed a motivation to combine or whether each limitation of the '786 Patent was disclosed in the prior art. *See* Pet. at 8-10. A motivation to combine inquiry must focus on whether a POSA would have been motivated to arrive at the specific invention claimed. *See Virtek Vision*, 97 F.4th at 886-887; *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015) (“Obviousness concerns whether a skilled artisan not only could have made but would have been motivated to make the combinations or modifications of prior art *to arrive at the claimed invention.*”) (cleaned up) (emphasis added). Likewise, whether the prior art discloses or teaches a claim necessarily depends on the specific claims at issue, and obviousness must be assessed on a claim-by-claim basis. *See MaxLinear*, 880 F.3d at 1377-78 (remanding where Board applied collateral estoppel to independent claims but failed to separately analyze dependent claims).

As discussed above, whether a POSA would have combined Gwozdz-PCT and Meezan to reach claims 1-27 of the '786 Patent or combined Gwozdz-PCT with Meezan and Cartt-784 to reach claims 20-21 are fundamentally different questions from whether the POSA would have done so for the '876 Patent. This distinction matters because every claim *of the specific inventions at issue* (i.e., those claimed in the '786 Patent) expressly recites *n*-dodecyl- β -D-maltoside, whereas the Board in the 451 IPR only addressed claims reciting “alkyl glycoside.” Moreover, Meezan emphasizes “highly branched” alkyl glycosides (which technically may be within the scope of “alkyl glycosides” of the '876 Patent claims) as preferred absorption enhancers, but does not teach a straight-chain compound like *n*-dodecyl- β -D-maltoside in the '786 Patent claims. “[A] difference in the claims that would alter a POSITA’s motivation to combine prior art references would be material to the invalidity analysis.” *See TQ Delta, LLC v. 2Wire, Inc.*, 2021 WL 2671296, at *6 (D. Del. June 29, 2021).

XIII. CONCLUSION

For the reasons above, the Board should conclude that Petitioner has failed to meet its burden of providing that Gwozdz-PCT, Cartt-784, and USP23/NF18 are prior art, that Gwozdz-PCT and Cartt-784 are available to be used as obviousness references, and that the combinations of prior art render obvious any claims of the '786 Patent.

Date: January 5, 2026

Respectfully submitted,

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CERTIFICATION OF WORD COUNT

The undersigned hereby certifies that the portions of the above-captioned PATENT OWNER'S RESPONSE specified in 37 C.F.R. §42.24 have 13,972 words, in compliance with the 14,000 word limit set forth in 37 C.F.R. §42.24. This word count was prepared using Microsoft Word 365 V.2503.

Dated: January 5, 2026

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing PATENT OWNER'S RESPONSE and supporting EXHIBITS 2034-2071, 2074, and 2076 were served on counsel of record for the Petitioner by filing this document through PTAB P-TACTS and by sending the same via electronic mail to the following addresses:

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