

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PADAGIS US LLC,
Petitioner,

v.

NEURELIS, INC.,
Patent Owner.

IPR2025-00466
Patent 11,793,786 B2

Before GRACE KARAFFA OBERMANN, ANNETTE R. REIMERS, and
TIMOTHY G. MAJORS, *Administrative Patent Judges*.

MAJORS, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Padagis US LLC (“Petitioner”) filed a Petition (Paper 2, “Pet.”) requesting *inter partes* review of claims 1–27 of U.S. Patent No. 11,793,786 B2 (Ex. 1001, “the ’786 patent”). Pet. 1, 6. Neurelis, Inc. (“Patent Owner”) filed a Preliminary Response (Paper 11, “Prelim. Resp.”).

Under 35 U.S.C. § 314(a), an *inter partes* review may not be instituted unless it is determined that there is a reasonable likelihood that the petitioner will prevail with respect to at least one of the claims challenged in the petition. For reasons explained below, we conclude that Petitioner shows a reasonable likelihood that it will prevail with respect to at least one of the ’786 patent’s challenged claims.¹ We institute *inter partes* review on all challenged claims. *SAS Inst. Inc. v. Iancu*, 584 U.S. 357, 362–63 (2018); 37 C.F.R. § 42.108(a) (“When instituting *inter partes* review, the Board will authorize the review to proceed on all of the challenged claims and on all grounds of unpatentability asserted for each claim.”).

Findings and conclusions at this stage are preliminary and based on the current record. Any final decision will be based on a full trial record.

II. BACKGROUND

A. *Real Parties-in-Interest*

Petitioner identifies Padagis LLC, Padagis US LLC, and Padagis Israel Pharmaceuticals Ltd. as the real parties-in-interest. Pet. 4. Patent Owner identifies itself as the real party-in-interest. Paper 3, 1.

¹ In a separate decision, the Acting Director denied Patent Owner’s request for discretionary denial of the Petition. Paper 12.

B. Related Matters

The parties identify the following lawsuit in which the '786 patent is asserted: *Neurelis, Inc. v. Padagis LLC et al.*, 1:24-cv-00562 (D. Del.).

Pet. 4; Paper 3, 1.

Other related matters are pending before the Board. Those matters include IPR2025-00464, challenging claims of U.S. Patent No. 8,895,546, and IPR2025-00465, challenging claims of U.S. Patent No. 11,241,414.

Paper 3, 1.

Petitioner also identifies IPR2019-00451 (“the 451 IPR”), which involved a different petitioner’s challenge to claims 1–36 of related U.S. Patent No. 9,763,876 (“the ’876 patent”).² Pet. 4. The 451 IPR resulted in a Final Written Decision dated August 6, 2020, in which the Board determined that claims 1–36 of the ’876 were unpatentable. Ex. 1040, 2–3, 68–69. On appeal by Patent Owner, the U.S. Court of Appeals for the Federal Circuit affirmed the Board’s Final Written Decision in the 451 IPR. Ex. 1068.

Patent Owner further identifies several pending patent applications as related to the ’786 patent. Paper 3, 1.

C. The ’786 Patent (Ex. 1001)

The ’786 patent is titled “Administration of Benzodiazepine Compositions.” Ex. 1001, code (54). The patent issued October 24, 2023, from an application filed April 12, 2021. *Id.* at codes (22), (45). The ’786 patent also claims the priority benefit of, among other applications, Non-Provisional Application No. 12/413,439, filed March 27, 2009, and Provisional Application No. 61/040,558, filed March 28, 2008 (“the ’558 Provisional” (Ex. 1008)). Ex. 1001, codes (60), (63).

² The ’876 patent is filed as Exhibit 1003 in related IPR2025-00464.

According to the '786 patent, the “invention relates to pharmaceutical compositions comprising one or more benzodiazepine drugs for nasal administration.” *Id.* at code (57).

As background, the '786 patent explains that benzodiazepines include “drugs such as diazepam, lorazepam, and medazepam,” which “have been observed as possessing sedative, tranquilizing and muscle relaxing properties.” *Id.* at 1:20–24. Such drugs “are thought to be useful in preventing, treating, or ameliorating the symptoms of anxiety, insomnia, agitation, seizures (such as those caused by epilepsy),” and other conditions. *Id.* at 1:25–31. Nonetheless, the patent acknowledges that development of formulations of benzodiazepine drugs “has been significantly limited due, in many cases, to solubility challenges.” *Id.* at 1:45–49.

The '786 patent states that, in embodiments of the invention, a composition for nasal administration comprises a benzodiazepine drug formulated into a carrier system comprising one or more natural or synthetic tocopherols or tocotrienols, and one or more alcohols or glycols. *Id.* at 6:7–20 (disclosing that the tocopherols and/or tocotrienols are present in an amount from about 30–95% (w/w) and the alcohols and/or glycols in an amount from about 5–70% (w/w)); *see also id.* at 6:27–34 (listing several benzodiazepine drugs including, *inter alia*, diazepam, midazolam, and lorazepam and pharmaceutically-acceptable salts and combinations thereof). According to the patent, “most benzodiazepines are so slightly soluble in water that a therapeutically effective amount cannot be dissolved in a volume of aqueous solvent that is amenable to application to the mucosal membrane.” *Id.* at 15:61–65. However, the patent states, by “use of the present carrier system, which in some embodiments, provides an improved ability to dissolve benzodiazepine drugs, the present invention allows

benzodiazepine drugs to be administered to one or more mucosal membranes, including to nasal mucosal membranes.” *Id.* at 15:65–16:3.

In further describing the carrier system, the ’876 patent states that the “inventors have found that Vitamin E [(which includes tocopherols and tocotrienols)] can provide an effective carrier for benzodiazepine drugs” such that, in embodiments, the “benzodiazepines are soluble, or partially soluble, in Vitamin E.” *Id.* at 30:37–44 (disclosing Vitamin E may also reduce mucosal irritation); *see also id.* 30:13–16 (disclosing Vitamin E refers to tocopherols or tocotrienols). Because Vitamin E is classified as hydrophobic, the patent also discloses the addition of “one or more lower alkyl alcohols or one or more lower alkyl glycols, or any combination thereof” in the carrier. *Id.* at 30:45–58 (identifying lower alcohols such as ethanol, propyl alcohol, and benzyl alcohol).

The ’786 patent discloses that embodiments of the pharmaceutical compositions may comprise additional excipients, including penetration enhancers. *Id.* at 30:64–65. According to the patent, “[i]n some embodiments, the penetration enhancer is at least one alkyl glycoside.” *Id.* at 30:67–31:1. The patent states that “[e]xemplary alkyl glycosides that may be employed include octyl . . . dodecyl . . . α - or β -D-maltoside, -glucoside or sucroside.” *Id.* at 31:17–20; *see also id.* at 32:33–34 (“In some embodiments, the alkyl glycoside is dodecyl maltoside.”), 53:21–28 (describing, for “Example 6,” that “[a]ll of the solutions and suspensions described in Examples 3 and 4 are formulated as described in Examples 3 and 4, with the addition of a suitable amount of an alkyl glycoside, as described herein, such as dodecyl maltoside, . . .”), 42:61–43:30 (Example 3 (Formulation of Diazepam Solutions) comprising Diazepam USP, Vitamin E USP, and dehydrated ethanol USP)).

D. Illustrative Claims

Petitioner challenges claims 1–27. Claims 1 and 11 are the only independent claims. Claim 1 is illustrative and is reproduced below:

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.

Ex. 1001, 54:64–55:11. Independent claim 11 is similar to claim 1 but omits the recitation of “tocotrienols” and variants thereof (e.g., α -tocotrienol, etc.). *Id.* at 55:45–57.

To illustrate the subject matter of some of the dependent claims, claim 20 depends from claim 1 and adds that “the therapeutically effective amount of diazepam or pharmaceutically acceptable salt thereof . . . is from about 5 to about 20 mg.” *Id.* at 56:30–34. Claim 26 depends from claim 1 and adds that “the α -tocopherol is Vitamin E USP.” *Id.* at 56:55–56.

E. Prior Art and Asserted Grounds

Petitioner asserts that claims 1–27 are unpatentable for obviousness based on the following grounds:

Grounds	Claims Challenged	35 U.S.C. §³	References/Basis
1	1–25	103	Gwozdz, ⁴ Meezan ⁵
2	20, 21	103	Gwozdz, Meezan, Cartt ⁶
3	26, 27	103	Gwozdz, Meezan, USP 23/NF 18 ⁷

Petitioner also relies on testimony from Maureen Donovan, Ph.D. (Ex. 1062) in support of its challenge.

³ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112–29, 125 Stat. 284, 285–88 (2011), revised 35 U.S.C. §§ 102, 103 effective March 16, 2013. The parties dispute whether the priority date for the challenged claims is March 28, 2008 (Patent Owner’s position), or no earlier than March 27, 2009 (Petitioner’s position). *See* Pet. 12–16; Prelim. Resp. 3. As both alleged priority dates precede the AIA’s effective date (March 16, 2013), we apply the pre-AIA versions of §§ 102 and 103 in this Decision.

⁴ Gwozdz et al., WO 2009/120933 A2, published Oct. 1, 2009 (Ex. 1009 (“Gwozdz”)).

⁵ Meezan et al., US 2006/0046962 A1, published Mar. 2, 2006 (Ex. 1010 (“Meezan”)).

⁶ Cartt et al., US 2008/0279784 A1, published Nov. 13, 2008 (Ex. 1065 (“Cartt”)).

⁷ USP 23/NF 18 1995, The Official Compendia of Standards, Vitamin E, Copyright 1994 (Ex. 1066 (“USP 23/NF 18”)).

III. ANALYSIS

A. *Legal Standards*

“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3)).

A claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the relevant art. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations (i.e., objective indicia) of nonobviousness when presented.⁸ *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

To show unpatentability based on a combination of teachings, “[a]n obviousness determination [also] requires finding both that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.” *CRFD*

⁸ Patent Owner mentions alleged “industry praise” and “commercial success” for the “Valtoco” drug product. Prelim. Resp. 18. But Patent Owner does not elaborate on these assertions or provide evidence to establish a nexus with the claimed subject matter. Thus, and for at least those reasons, the assertions of industry praise and commercial success are entitled to no weight as objective indicia of nonobviousness at this stage.

Rsch., Inc. v. Matal, 876 F.3d 1330, 1340 (Fed. Cir. 2017) (internal quotation marks omitted).

B. Level of Ordinary Skill in the Art

Petitioner proposes that the person of ordinary skill in the art (“POSA”) at the earliest effective filing date of the ’786 patent would have had the following qualifications:

[A POSA] would have been a pharmaceutical scientist, chemist, or biologist involved in the research and development of pharmaceutical formulations and/or delivery, and would have at least a Bachelor’s degree with at least 5 years of experience, or a Master’s, Ph.D. or Pharm.D. degree with several years of experience. In addition, . . . a POSA would have had knowledge of benzodiazepine structure and function, and would further have knowledge and practical experience working with intranasal and transmembrane formulations, including knowledge of the physiology and anatomy of the nasal cavity, with relevant experience in developing intranasal formulations.

Pet. 26; Ex. 1062 ¶ 20. Patent Owner “does not dispute” Petitioner’s POSA definition at this stage. Prelim. Resp. 19.

We apply Petitioner’s proposed POSA definition for this Decision, which definition appears to be generally consistent with the cited prior art.

C. Claim Construction

In an IPR, we construe claims using the same claim construction standard used in a civil action before the courts under 35 U.S.C. § 282(b), including construing claim language in accordance with its ordinary and customary meaning as understood by the POSA, in view of the patent’s specification and considering the patent’s prosecution history. 37 C.F.R. § 42.100(b). We need only expressly construe terms to the extent needed to resolve the controversy before us. *Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1375 (Fed. Cir. 2019).

Petitioner argues “the Board should construe ‘vitamin E’ as expressly defined to mean ‘any of the natural or synthetic tocopherols, tocotrienols, any isomers thereof, any esters thereof, any analogs or derivatives thereof, or any combinations thereof.’” Pet. 17 (quoting Ex. 1001, 30:13–16).⁹

According to Patent Owner, “no construction is required, as this term has a plain and ordinary meaning to a person of ordinary skill in the art.”¹⁰

Prelim. Resp. 19.

The ’786 patent does appear to define “vitamin E” consistent with Petitioner’s proposed construction. Ex. 1001, 30:13–16. There is, however, no issue at this stage that turns on a disputed meaning of “vitamin E” or any of the other claim terms. Accordingly, we need not at this time expressly construe the term “vitamin E.” *Realtime Data*, 912 F.3d at 1375.

⁹ In Petitioner’s obviousness analysis, Petitioner suggests the transitional phrase “consisting of” means the claimed pharmaceutical solutions include only those components recited in the claims. *See, e.g.*, Pet. 36 (noting “consisting of” means “containing only”). Such interpretation tracks the conventional meaning of the “consisting of” transitional phrase in claim drafting. *See AFG Indus., Inc. v. Cardinal IG Co.*, 239 F.3d 1239, 1245 (Fed. Cir. 2001) (“[C]losed transition phrases such as ‘consisting of’ are understood to exclude any elements, steps, or ingredients not specified in the claim.”). It is also consistent with the ’786 patent’s definition of the “consisting of” phrase. Ex. 1001, 15:34–36 (“As used herein, the term ‘consisting of’ . . . indicate[s] that the claimed invention includes only those elements set forth in the claim.”).

¹⁰ The Preliminary Response attributes this “no construction” assertion as coming from “Petitioner.” Prelim. Resp. 19. In context, however, we understand this reference to “Petitioner” to be a typographical mistake and that Patent Owner was providing its own position about whether the term “vitamin E” requires construction.

D. Asserted References

Petitioner asserts that Gwozdz and Cartt are prior art to the '786 patent under 35 U.S.C. § 102(e), and that Meezan and USP 23/NF 18 are prior art under 35 U.S.C. § 102(b). Pet. 21–26.

Patent Owner does not dispute the prior art status of Meezan, Cartt, or USP 23/NF 18. As discussed below, Patent Owner argues Gwozdz is not prior art because the challenged claims are allegedly entitled to the March 28, 2008, priority date of the '558 Provisional. *See infra* Section III.E. Patent Owner also contends that one portion of Gwozdz's disclosure cited by Petitioner is not prior art irrespective to whether the challenged claims are entitled to the March 28, 2008, priority date. *See infra* Section III.F.2.

1. Gwozdz (Ex. 1009)

Gwozdz is a published PCT application, filed March 27, 2009, and published October 1, 2009. Ex. 1009, codes (22), (43). Gwozdz claims the priority benefit of U.S. Provisional Application No. 61/040,281, filed March 28, 2008 ("the Gwozdz Provisional" (Ex. 1064)). Ex. 1009, code (30).

Gwozdz is titled "Pharmaceutical Solutions and Method for Solubilizing Therapeutic Agents." *Id.* at code (54). Gwozdz discloses that "[p]harmaceutical solutions containing hydrophobic or lipophilic therapeutic agents . . . are produced by dissolving the therapeutic agent in one or more tocopherols or tocotrienols and one or more alcohols or glycols," which solutions "are used to produce pharmaceutical compositions." *Id.* at code (57). As background, Gwozdz identifies "diazepam" as an example lipophilic or hydrophobic therapeutic agent known to be "water insoluble or poorly water soluble." *Id.* at 1:10–19.

Gwozdz discloses that, in embodiments of its pharmaceutical solutions, "the tocopherol(s) and/or tocotrienol(s) is in an amount from about

30% to about 99% (w/w) and the alcohol(s) and/or glycol(s) is in an amount from about 1% to about 70% (w/w).” *Id.* at 4:13–21; *see also id.* at 5:11–14 (disclosing that the therapeutic agent is dissolved in the tocopherol and/or tocotrienol and an alcohol and/or glycol as solvents), 7:20–28 (preferred amounts and ratios of solvent components). According to Gwozdz, tocopherols and tocotrienols include the family of natural and synthetic compounds “also known by the generic names tocols or vitamin E.” *Id.* at 5:33–6:2. Gwozdz further discloses that example alcohols for use in the solutions include, among others, “ethanol,” “propyl alcohol,” and “benzyl alcohol,” and “any combinations thereof.” *Id.* at 6:16–23.

Gwozdz discloses that solutions including the one or more tocopherols and/or tocotrienols and one or more alcohols and/or glycols “are used in the solubilization of hydrophobic or lipophilic therapeutic agents thereby providing increased bioavailability of the therapeutic agent.” *Id.* at 7:3–8. Gwozdz teaches exemplary therapeutic agents that can be solubilized include, *inter alia*, “benzodiazepines such as Diazepam.” *Id.* at 8:6–18. Gwozdz teaches that its pharmaceutical solutions “are particularly useful in formulations to be administered to mucosal membranes, i.e., the nasal mucosa or lungs of a subject by any suitable means.” *Id.* at 9:19–10:2 (disclosing that the solutions “provide[] for improved ability to dissolve hydrophobic and lipophilic therapeutic agents” and the solutions can be administered with, for example, “a metered dose inhaler or nebulizer, or in a mist sprayer”).

2. *Meezan (Ex. 1010)*

Meezan is a published U.S. patent application, which was published March 2, 2006. Ex. 1010, code (43).

Meezan is titled “Absorption Enhancers for Drug Administration.” *Id.* at code (54). As background, Meezan discloses that therapeutic agents are often combined with various surfactants but surfactants can be irritating to mucosal tissues, such as found in the nose, mouth, or eyes. *Id.* ¶ 3. According to Meezan, “an ideal enhancing surfactant” will stabilize the therapeutic agent, be non-toxic and non-irritable, and “enhance the passage or absorption of the therapeutic agent through various membrane barriers without damaging the structural integrity and biological function of the membrane and increase bioavailability of the agent.” *Id.*

Meezan discloses

a method of increasing absorption of a low molecular weight compound into the circulatory system of a subject by administering the compound via the oral, ocular, nasal, nasolacrimal, inhalation or pulmonary, oral cavity . . . , or CSF delivery route when admixed, mixed or blended with an absorption increasing amount of a suitable surfactant, wherein the surfactant is a nontoxic and nonionic hydrophobic alkyl joined by a linkage to a hydrophilic saccharide.

Id. ¶ 8. Meezan discloses that therapeutic agents and drugs suitable for use with its invention may include small to medium size peptides or proteins, and further “methods of the invention also anticipate the use of small molecules, for example, an organic compound that has a molecular weight of less than 3 kD, or less than 1.5 kD.” *Id.* ¶ 130.

According to Meezan, the surfactant of the invention preferably “consists of at least one suitable alkyl glycoside.” *Id.* ¶ 54. Meezan discloses that “[a]llyl glycosides of the present invention can include, but are not limited to: alkyl glycosides, such as octyl-, nonyl-, decyl-, undecyl-, dodecyl-, tridecyl-, . . . and octadecyl- α - or β -D-maltoside, -glucoside or sucroside.” *Id.* ¶ 56; *see also id.* ¶¶ 58 (disclosing “preferred glycosides

include maltose, sucrose, and glucose linked by a glycosidic linkage to an alkyl chain of 9, 10, 12, 13, 14, 16, 18, 20, 22, or 24 carbon atoms, e.g., nonyl-, decyl-, dodecyl- and tetradecyl sucroside, glucoside, and maltoside, etc.”), 61 (“preferred glycosides can include maltose” linked to an “alkyl chain of about 9-16 carbons” such as dodecyl maltoside). In examples, Meezan discloses a use of dodecyl maltoside as the surfactant. *Id.* ¶¶ 153–159 (Example 3 (administration of insulin via ocular route); Table I (eye drops containing insulin and various concentrations of dodecyl maltoside)); *see also id.* ¶ 158 (“The effects of the alkylmaltosides as absorption enhancers are dose-dependent.”).

Meezan discloses that “surfactant compositions of the invention are typically present at a level of from about 0.01% to 20% by weight.” *Id.* ¶ 70. Meezan also discloses that therapeutic compositions of the invention can be administered through a variety of routes including, for example, “ocular” and “nasal” routes and that the mode of delivery (e.g., liquid, spray, etc.) depends on the method of delivery to the subject. *Id.* ¶ 73. According to Meezan, the therapeutic compositions may include an acceptable carrier, such as “an aqueous or non-aqueous agent, for example alcoholic or oleaginous, or a mixture thereof.” *Id.* ¶ 74 (“A pharmaceutically acceptable carrier can also be selected from substances such as distilled water, benzyl alcohol, lactose” or other substances.).

3. *Cartt (Ex. 1065)*

Cartt is a published U.S. patent application, which was published November 13, 2008, from an application filed May 7, 2008. Ex. 1065, codes (22), (43). Cartt claims the priority benefit of U.S. Provisional Application No. 60/916,550, filed May 7, 2007 (“the Cartt Provisional” (Ex. 1067)).

Cartt is titled “Nasal Administration of Benzodiazepines” and relates generally to formulations of benzodiazepines, such as diazepam, for nasal administration to patients. *Id.* at codes (54), (57) (“nasal administration for the treatment of seizure”). Cartt discloses that diazepam is a drug with anticonvulsive, sedative, and muscle relaxant properties and “it is expected that a therapeutic dose will be in the range of about 1 to about 20, preferably about 2 to about 10 mg per dose.” *Id.* ¶ 63.

4. *USP 23/NF 18 (Ex. 1066)*

USP 23/NF 18 includes excerpts from the 1995 United States Pharmacopeia, The National Formulary. *See generally*, Ex. 1066. The excerpts, which comprise an official monograph for, *inter alia*, Vitamin E, disclose that “Vitamin E is a form of alpha tocopherol (C₂₉H₅₀O₂)” and variants. *Id.* at 1631 (“It contains not less than 96.0 percent and not more than 102.0 percent of C₂₉H₅₀O₂, C₃₁H₅₂O₃, or C₃₃H₅₄O₅, respectively.”).

E. *Prior-Art Status of Gwozdz & Priority Date of the Challenged Claims*

1. *Overview of the Priority Dispute*

Petitioner contends that Gwozdz is prior art as of the March 28, 2008, filing date of the Gwozdz Provisional.¹¹ Pet. 21–23. In support, Petitioner argues Gwozdz’s claims match the claims in the Gwozdz Provisional, and Petitioner maps the relied-upon disclosures in Gwozdz to corresponding disclosures in the Gwozdz Provisional. *Id.* at 21–22. Thus, Petitioner argues that, applying the framework in *Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375 (Fed. Cir. 2015), Gwozdz qualifies as § 102(e) prior art with an effective date of March 28, 2008. Pet. 22–23.

¹¹ The Gwozdz Provisional and the ’558 Provisional (to which the ’786 patent claims priority) were both filed the same day—March 28, 2008.

Patent Owner does not at this time contest that Gwozdz is entitled to the filing date of the Gwozdz Provisional except for the disclosure of one phrase in Gwozdz. Prelim. Resp. 37–39 (arguing the phrase “penetration enhancers” in a listing of additives on page 10 of Gwozdz is missing in the corresponding listing of additives in the Gwozdz Provisional). We address that phrase in Section III.F.2 below, but we otherwise find that Petitioner has made a threshold showing that Gwozdz’s effective date is March 28, 2008.

Petitioner further argues that the challenged claims are not entitled to priority to the March 28, 2008, filing date of the ’558 Provisional. Pet. 12–16. Petitioner notes that all the challenged claims require, as a component of the claimed pharmaceutical solutions, an alkyl glycoside—and specifically “n-dodecyl beta-D maltoside.” *Id.* at 13. According to Petitioner, however, the “first mention” of “alkyl glycosides . . . (or any species thereof, e.g., dodecyl maltoside)” in the ancestral applications to which the ’786 patent claims priority is in the ’439 Application, filed March 27, 2009. *Id.* at 13–14 (citing Ex. 1039 ¶¶ 18, 43, 47, 56; illustrating family tree for the ’786 patent and other related patents/applications). Petitioner argues “[t]here is not a single recitation of the terms ‘alkyl glycoside’ or ‘maltoside’ anywhere in the specification of the [earlier-filed] ’558 Provisional.” *Id.* So, Petitioner contends, the ’558 Provisional does not provide written description support for the challenged claims and those claims are not entitled to a priority date that is earlier than March 27, 2009. Pet. 13–14.

Petitioner, recognizing that the ’558 Provisional purports to incorporate-by-reference several pages from a “SIGMA Catalog,” contends that the ’558 Provisional is nonetheless ineffective in providing a sufficient written description for the challenged claims. Pet. 14–15; *see* Ex. 1026 (SIGMA Catalog); Ex. 1008 ¶ 152 (“In some embodiments, enhancing

agents that are appropriate include chelating agents (EGTA, EDTA, alginates), surface active agents (especially non-ionic materials), acyl glycerols, fatty acids and salts, tyloxapol and biological detergents listed in the SIGMA Catalog, 1988, page 316-321 (which is incorporated herein by reference).”). In support, Petitioner makes three arguments, which we summarize below.

First, insofar as the SIGMA Catalog lists many detergents, some of which are alkyl glycosides and one that is n-dodecyl beta-D-maltoside, Petitioner contends that Patent Owner cannot rely on such disclosures to provide written description support for the claims. Pet. 15. According to Petitioner, 37 C.F.R. § 1.57(d) (“Rule 1.57(d)”) prohibits the incorporation-by-reference of “essential material” (i.e., material necessary to supply written description support for the claimed invention) from non-patent publications like the SIGMA Catalog. *Id.* (citing 37 C.F.R. § 1.57(d)).

Second, Petitioner argues that, based on results from the 451 IPR, collateral estoppel forecloses Patent Owner from relitigating whether content in the SIGMA Catalog provides written description support for the claims. Pet. 8–9, 13. According to Petitioner, collateral estoppel applies “even when claims are not identical so long as the issues are materially the same.” *Id.* at 8 (citing, e.g., *Finjan LLC v. SonicWall, Inc.*, 84 F.4th 963, 969 (Fed. Cir. 2023)). And, Petitioner argues, materially the same issue was already litigated in the 451 IPR when the Board determined in a final decision (affirmed on appeal) that, even if the SIGMA Catalog was incorporated by reference, “the ’558 Provisional does not provide adequate written description support for the ‘alkyl glycoside limitation.’” *Id.* at 13 (quoting, with Petitioner’s emphasis, Ex. 1040 (Final Decision in IPR2019-00451), 23).

Third, Petitioner argues that the collective disclosures of the '558 Provisional and the SIGMA Catalog (assuming it is incorporated-by-reference) fail to provide sufficient written description support for the claims. Citing the testimony of Petitioner's declarant, Dr. Donovan, Petitioner contends that the '558 Provisional identifies numerous chemical classes of potential "enhancers," only one class of which are "biological detergents." *Id.* at 15 (citing, e.g., Ex. 1062 ¶¶ 46–53; Ex. 1008 ¶¶ 150–152). And, even with the SIGMA Catalog's disclosure of 100-plus possible detergents, Petitioner contends that there is no direction or guidance that would have led the ordinarily skilled artisan to the use of alkyl glycosides or, in particular, n-dodecyl beta-D-maltoside, for the claimed pharmaceutical solutions. *Id.* at 15–16 (citing, e.g., Ex. 1062 ¶¶ 50–53 (testifying, *inter alia*, that only a small portion (about a dozen) of the more than 150 ionic and non-ionic compounds in the SIGMA Catalog are alkyl glycosides, with no guidance to select n-dodecyl beta-D-maltoside)).¹²

Patent Owner responds that Gwozdz is not prior art because the challenged claims are entitled to a priority date that is at least as early as the Gwozdz Provisional. Prelim. Resp. 21–33. According to Patent Owner, the claims are entitled to priority to the filing date of the '558 Provisional (March 28, 2008) as that application incorporates-by-reference portions of the SIGMA Catalog and provides written description support for the claims. *Id.*; *see also id.* at 25–27 (emphasizing, *inter alia*, that the '558 Provisional,

¹² Dr. Donovan further testifies that, without appropriate guidance in the '558 Provisional (inclusive of the cited pages of the SIGMA Catalog), "it would require the POSA to conduct undue experimentation to determine whether any of the alkyl glycosides are useful or preferred over any of the other biological detergent candidates." Ex. 1062 ¶ 51.

by its incorporation of the SIGMA Catalog, expressly includes n-dodecyl beta-D-maltoside among its listed detergents). Patent Owner argues that Rule 1.57(d) does not apply when the incorporation relates to entitlement to a priority-benefit claim to an earlier-filed ancestral application. *Id.* at 27–28 (citing MPEP § 608.01(p)(I)(B)). Patent Owner also argues that collateral estoppel does not bar Patent Owner from arguing that the challenged claims here are entitled to priority to the ’558 Provisional. *Id.* at 23–25. According to Patent Owner, the test for invoking collateral estoppel is unmet because the priority issue here versus the 451 IPR is not identical, nor was the same issue actually litigated in the 451 IPR—the ’786 patent’s claims all require “n-dodecyl beta-D-maltoside,” not merely an “alkyl glycoside.” *Id.* (arguing the Board in the 451 IPR decided the written description and priority issue more broadly as to whether the “alkyl glycoside” limitation was supported (citing Ex. 1040, 14 n.6, 19 n.7, 23)).

2. Rule 1.57(d)

Rule 1.57(d) recites, in pertinent part, that “[e]ssential material’ may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication, which patent or patent application does not itself incorporate such essential material by reference.” 37 C.F.R. § 1.57(d). Further, “[e]ssential material” is material necessary to “[p]rovide a written description of the claimed invention . . . as required by 35 U.S.C. 112(a).” *Id.*

Petitioner argues that, under Rule 1.57(d), “[w]ritten description support cannot be provided by incorporation by reference to non-patent literature.” Pet. 15. Because the SIGMA Catalog is non-patent literature, Petitioner argues the ’558 Provisional cannot incorporate that catalog’s

contents by reference to establish written description support for the challenged claims of the '786 patent. *Id.*

We need not at this time decide whether Rule 1.57(d) applies in the manner urged by Petitioner. As we discuss below, on the current record and even assuming the relevant pages of the SIGMA Catalog are incorporated into the '558 Provisional, we find that Petitioner has made a threshold showing that written description support for the challenged claims is lacking.

Notwithstanding the above, if the applicability of Rule 1.57(d) remains at issue throughout trial, the parties should each address whether Office guidance otherwise allows applications that are relied on *only for a priority-benefit claim* to incorporate essential material by reference—whether the incorporation be from patent or non-patent literature. The MPEP's Section 608.01(p) provides, for example:

The limitations on 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 under 35 U.S.C. 119 or 35 U.S.C. 120. 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).

MPEP § 601.01(p) (9th Ed. Rev. 01.2024 Nov. 2024) (“Incorporation by reference in the earlier application of . . . (2) nonpatent publications, (3) a U.S. patent or application which itself incorporates ‘essential material’ by

reference . . . ***is not critical*** in the case of a ‘benefit’ application.”) (emphasis added).¹³ We will revisit this issue, if needed, on a complete record.

We address one further assertion made by Patent Owner concerning Rule 1.57(d). Patent Owner characterizes Petitioner’s Rule 1.57(d) argument as “disingenuous” given the 451 IPR record. Prelim. Resp. 28 (arguing the incorporation-by-reference of the SIGMA Catalog “was found ***sufficient***” in the 451 IPR (citing Ex. 2029 (excerpts of oral argument before the Federal Circuit), 12:3–8)). We disagree with that characterization. In the Final Written Decision from the 451 IPR, the Board *did not decide* the Rule 1.57(d) issue and instead simply “assum[ed]” the SIGMA Catalog was properly incorporated. Ex. 1040, 19 n.7 (“For purposes of this Decision, we do not need to decide the Rule 57 issue.”). Moreover, the colloquy before the Federal Circuit cited by Patent Owner does not mention Rule 1.57 and, in any event, a different petitioner’s concession about whether the SIGMA Catalog was considered incorporated does not bind *this Petitioner*.

3. Collateral Estoppel

“It is well established that collateral estoppel, also known as issue preclusion, applies in the administrative context.” *Nestlé USA, Inc. v. Steuben Foods, Inc.*, 884 F.3d 1350, 1351–52 (Fed. Cir. 2018) (quoting

¹³ The parties may also consider addressing other Board decisions where the interplay between Rule 1.57 and MPEP 608.01(p) is discussed. *See, e.g., Neurent Medical Inc. v. The Foundry, LLC*, IPR2024-00669, Paper 8 at 21–22 (PTAB July 23, 2024) (finding, at institution, that a putative priority-benefit application may incorporate-by-reference essential material from a separate provisional application); *Samsung Elecs. v. Acquis LLC*, IPR2021-00608, Paper 10 at 8–10 (PTAB Dec. 8, 2021) (addressing a priority application’s nested incorporation-by-reference of essential material and explaining that the Office has maintained the guidance in MPEP § 608.01(p) even after Rule 1.57(d) became effective).

MaxLinear, Inc. v. CF CRESPE LLC, 880 F.3d 1373, 1376 (Fed. Cir. 2018) and applying collateral estoppel to vacate a claim construction in an underlying IPR). In an IPR, “a party seeking to invoke collateral estoppel must show: ‘(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 LLC v. Hammond Development Int’l, Inc.*, 54 F.4th 1377, 1381 (Fed. Cir. 2022) (quoting *In re Freeman*, 30 F.3d 1459, 1465 (Fed. Cir. 1994)) (alteration in original).¹⁴

“It is [also] well established that patent claims need not be identical for collateral estoppel to apply.” *Id.* at 1381. Instead, “collateral estoppel requires the *issues of patentability* be identical.” *Id.* If “the differences between the unadjudicated patent claims and adjudicated patent claims do not materially alter the question of invalidity, collateral estoppel applies.” *Ohio Willow Wood Co. v. Alps South, LLC*, 735 F.3d 1333, 1342–43 (Fed. Cir. 2013) (affirming application of collateral estoppel where claims adjudicated as obvious required a “polymeric” gel whereas similar, unadjudicated claims required a “block copolymer” gel). “Collateral estoppel also applies to common issues in actions involving different but related patents.” *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 252 F.3d 1306, 1310 (Fed. Cir. 2001), *vacated on other grounds*, 353 U.S. 1109 (2002).

¹⁴ Some precedents use slightly different phrasing for parts of the collateral estoppel test. For example, in *VirnetX Inc. v. Apple, Inc.*, 909 F.3d 1375, 1377 (Fed. Cir. 2018), the court described part (2) as follows: “(2) the prior action actually litigated and adjudged that issue.”

According to Petitioner, “the issues presented in this Petition are substantially the same as the issues the Board previously considered in IPR2019-00451” when the Board held that the claims of the related ’876 patent were unpatentable. Pet. 1. Petitioner argues that collateral estoppel applies, including on the issue whether the ’558 Provisional provides written description support for similar claims challenged here. *Id.* at 1–3, 8–9 (arguing collateral estoppel applies based on the Board’s finding that the ’558 Provisional “does not provide adequate written description support for the ‘alkyl glycoside’ limitation” (citing Ex. 1040, 23)); *see also id.* 13 (“Patent Owner is collaterally estopped from contesting this [written description] finding” from the 451 IPR). Petitioner provides a side-by-side comparison of the challenged claims of the ’786 patent versus claims held unpatentable in the 451 IPR. *Id.* at 2–3 (citing Ex. 1069 (chart comparing claims 1–9 and 11–25 of the ’786 patent to claims 1–36 of the ’876 patent)). Petitioner argues the “primary difference” between the adjudicated and unadjudicated claims is the former are directed to a method of treatment using a pharmaceutical solution while the latter are directed to the pharmaceutical solution itself. *Id.* at 1–2. As that difference is allegedly immaterial, Petitioner contends collateral estoppel bars Patent Owner from arguing that the challenged claims are entitled to priority to the filing date of the ’558 Provisional. *Id.* at 1–3, 6–10, 13.

On the present record, 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. Comparing claim 1 of the ’876 patent to claim 1 of the ’786 patent reveals more differences than simply a method of using a pharmaceutical solution and the pharmaceutical solution itself. The

pharmaceutical solution in claim 1 of the '876 patent recites, among other components, “an alkyl glycoside” while the solution in claim 1 of the '786 patent requires a species of alkyl glycoside—“n-dodecyl beta-D-maltoside.” *See* Ex. 1069, 1 (gray-colored limitations); Prelim. Resp. 23 (arguing every claim in this proceeding requires “n-dodecyl beta-D-maltoside as a component of the pharmaceutical solution”). 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. And whether the '558 Provisional provides a sufficient written description for a pharmaceutical solution that includes a species of alkyl glycoside (i.e., n-dodecyl beta-D-maltoside) compared to a description sufficient to show possession of the use of pharmaceutical solutions that include a broader genera of alkyl glycosides may present materially distinct issues. In the 451 IPR, the Board decided the description and priority issue more broadly, addressing the claimed genera of “an alkyl glycoside.” Prelim. Resp. 23–24 (citing Ex. 1040, 23); *see also* Ex. 1040, 14 n.6, 19 n.7.

We note, as pointed out by Patent Owner, that “there were claims of the '876 Patent [in the 451 IPR] that required ‘dodecyl maltoside.’” Prelim. Resp. 24; Ex. 1069, 2 (e.g., dependent claim 26). But presaging argument Petitioner might raise about those other claims, Patent Owner contends it would still be improper to “interpolate that the priority issue relevant to the '786 Patent was decided.” Prelim. Resp. 24–25. Patent Owner argues the parties in the 451 IPR never joined battle and litigated to a final adjudication by the Board the issue whether the '558 Provisional supported “dodecyl maltoside” recited in some of the '876 patent’s dependent claims. *Id.* (citing Ex. 2028, 64 (petitioner from the 451 IPR asserting on appeal that Patent

Owner waived argument before the Board that the SIGMA Catalog’s listing of dodecyl maltoside provides written description for dependent claims)).

The record is ambiguous in showing that, during the 451 IPR, the parties joined issue and actually litigated the sufficiency of written description support for those dependent claims reciting dodecyl maltoside. *First*, in the 451 IPR trial proceedings, Patent Owner’s only separate suggestion of adequate written description for the subject dependent claims appears to have been relegated to a footnote. *See* Ex. 2029, 2 (Chief Judge Moore of the Federal Circuit asking about waiver and suggesting Patent Owner’s position before the Board on the dependent claims “was made only in a single footnote in passing and [was] not a developed argument”); IPR2019-00451, Paper 16 (Patent Owner Response) at 19 n.7.

Second, it is unclear that the Board saw the sufficiency of written description support for those dependent claims as being an issue joined by the parties that was resolved on the merits against Patent Owner, or whether the Board saw the issue as waived by Patent Owner for lack of developed counterargument.¹⁵ Either way, the Board’s decision in the 451 IPR only *explicitly* found written description inadequate for the “alkyl glycoside” limitation. Ex. 1040, 23 (“[W]e find that the ’558 provisional does not provide adequate written description support for the ‘alkyl glycoside’

¹⁵ As the Federal Circuit explains, collateral estoppel does not apply to issues that might have been but were not actually litigated and determined in a prior action. *Purdue Pharma L.P. v. Iancu*, 767 F. App’x 918, 922 (Fed. Cir. 2019) (citing the Restatement (Second) of Judgments for the proposition that issues are “not actually litigated” if, for example, they not denied in a responsive pleading, or if based on stipulations, consent, or default); Restatement (Second) of Judgments § 27, cmt. e (Am. Law. Inst. 1982).

limitation. Therefore, the claims of the '876 patent are not entitled to the benefit of priority to the '558 provisional.”).

Accordingly, even if the adequacy of written description support for “dodecyl maltoside” (in some claims challenged previously) and “n-dodecyl beta-D-maltoside” (in the challenged claims here) raised the same issue, Petitioner has not shown that issue was actually litigated and decided in the 451 IPR. Where the same issue is not actually litigated and decided in an earlier action, the test for invoking collateral estoppel in a later action is unmet. On this record and for the reasons above, we are unpersuaded that collateral estoppel bars Patent Owner from arguing the challenged claims are entitled to the priority date of the '558 Provisional.

4. *Whether the '558 Provisional Provides a Written Description of the Challenged Claims*

Whether claims are entitled to the priority benefit of an earlier effective filing date is based on disclosure of the invention “in the manner provided by section 112(a)” in a related and earlier-filed application. *See* 35 U.S.C. §§ 119(e), 120. “[A] patent’s claims are not entitled to an earlier priority date merely because the patentee claims priority. . . . Rather, for a patent’s claims to be entitled to an earlier priority date, the patentee must demonstrate that the claims meet the requirements of 35 U.S.C. § 120,” which include satisfying the written description requirement of § 112. *In re NTP, Inc.*, 654 F.3d 1268, 1276–77 (Fed. Cir. 2011) (citations omitted).

“The essence of the written description requirement is that a patent applicant, as part of the bargain with the public, must describe his or her invention so that the public will know what it is and that he or she has truly made the claimed invention.” *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1298 (Fed. Cir. 2014). “[T]he test for

sufficiency [of the written description requirement] is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date sought.” *Ariad Pharm., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (explaining that “the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed”) (internal quotation marks omitted); *see also id.* at 1352 (“[A] description that merely renders the invention obvious does not satisfy the requirement.”).

Petitioner argues that, even if the SIGMA Catalog is incorporated into the ’558 Provisional, adequate written description for the claims is missing. Pet. 15–16. Petitioner contends that the ’558 Provisional discloses a use of “enhancers . . . but only generally” and without guidance directing the POSA to the use of any alkyl glycosides. *Id.* at 15. Indeed, Petitioner contends, the ’558 Provisional discloses “at least fifteen different chemical classes of enhancers, one of which are the biological detergents listed in the 1998 SIGMA Catalog.” *Id.* Petitioner argues that, considering the six cited pages of the SIGMA Catalog, there are “over 100 biological detergents” with no meaningful direction that would have led the POSA to select alkyl glycosides or n-dodecyl beta-D-maltoside in particular for a pharmaceutical solution as recited in claim 1 of the ’786 patent. *Id.* at 15–16.

Petitioner reinforces its argument about the lack of written description support with Dr. Donovan’s testimony, which is substantively unrebutted at this time. Ex. 1062 ¶¶ 46–53 (testifying, *inter alia*, that given the disclosure of over fifteen classes of potential chemical enhancers and the SIGMA Catalog’s listing of “more than 150 ionic and non-ionic compounds” (within a class of detergents), the ’558 Provisional provides insufficient guidance

pointing to a selection and use of n-dodecyl beta-D-maltoside); *see also id.* ¶ 52 (analyzing paragraphs 150–152 of the ’558 Provisional along with the SIGMA Catalog, and opining “that the inventors did not have any particular enhancing agent in mind as part of their invention (other than paragraph [151]’s preference for lysophospholipids and acyl carnitine alternatives)”).

We find that Petitioner has made a threshold showing that the ’558 Provisional does not provide written description support for claim 1’s pharmaceutical solution consisting of each of the recited elements, including n-dodecyl beta-D-maltoside. It is true that “n-Dodecyl β -D-maltoside” can be found listed in the SIGMA Catalog. Ex. 1026, 316. But Dr. Donovan’s testimony helps put that listing in context. It is merely one among well over 100 ionic and non-ionic detergents listed in the cited six pages of the SIGMA Catalog. *See* 1026, 316–321; Ex. 1062 ¶ 50. When further considered in the context of paragraphs 150–152 of the ’558 Provisional, which generically suggest that “enhancer” compounds can be used in “some embodiments”—then introducing at least 15 classes of potential enhancers¹⁶ including “preferred” lysophospholipids and acyl carnitines—the listing of n-dodecyl beta-D-maltoside among at least 150 biological detergents in the SIGMA Catalog is even more remote.

Moreover, although satisfaction of the written description requirement is not limited to what is exemplified in a priority application, none of the ’558 Provisional’s examples use any “enhancer,” much less any detergent, any alkyl glycoside, or n-dodecyl beta-D maltoside in particular. The

¹⁶ The ’558 Provisional suggests that whether “a given compound” will function as an “enhancer” in a formulation requires testing. Ex. 1008 ¶ 150 (indicating “an in vivo or good model test” may “determin[e] whether the uptake of the drug is enhanced to a clinically significant degree”).

'558 Provisional's working examples include diazepam, α -tocopherol, and ethanol. *See* Ex. 1008 ¶¶ 172–174 (Examples 1 and 2).

In short, we find no sufficient disclosure of “blaze marks” in the '558 Provisional that point to the inventors' possession of a pharmaceutical solution that includes n-dodecyl beta-D-maltoside as claimed. *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326–27 (Fed. Cir. 2000) (analogizing an application's generic disclosures to a forest of unmarked trees and explaining that, “to satisfy the written description requirement,” there must be “blaze marks directing the skilled artisan to that tree [within the forest that represents the claimed invention]” in the application).

We have considered Patent Owner's counterarguments, but they are unavailing at this stage.

Patent Owner argues that, because “n-Dodecyl β -D-maltoside” is found in the SIGMA Catalog's listing of detergents, the written description requirement is “indisputabl[y]” met. Prelim. Resp. 26–27. We disagree. Patent Owner does not address the context in which that listing appears, as discussed above. Nor does Patent Owner provide evidence that persuasively rebuts Dr. Donovan's testimony to show why the skilled artisan would understand the inventors possessed the invention as recited in the challenged claims. *Ariad*, 598 F.3d at 1352 (explaining that the written description's “possession” test “requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art”).

Furthermore, that “n-Dodecyl β -D-maltoside” may appear in the '558 Provisional (by virtue of the alleged incorporation of the SIGMA Catalog) is not necessarily decisive. In *Fujikawa*, for example, a claim to a sub-genus of chemical compounds having specific R-position substitutions (i.e., R=cyclopropyl and R₀=4-fluorophenyl) was found to lack a sufficient

written description despite the Specification disclosing those substitutions as possibilities. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570–71 (Fed. Cir. 1996) (listing methyl and isopropyl, rather than cyclopropyl, as “preferred” moieties for R; and 4-fluorophenyl listed among three preferred choices for R₀). In affirming the Board, 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. *Id.* at 1571 (“[J]ust because a moiety [(e.g., cyclopropyl)] is listed as one possible choice for one position [(i.e., R)] does not mean there is *ipsis verbis* support for every species or sub-genus that chooses that moiety” and noting that, were it otherwise, “laundry list” disclosures of possibilities would suffice).

According to Patent Owner, the ’558 Provisional also discloses that the compositions may include “enhancers.” Prelim. Resp. 28–29 (citing, e.g., Ex. 1008 ¶¶ 16, 150, claim 17). As explained above, however, such disclosure is generic and, at this stage, we find no blaze marks pointing to the addition of n-dodecyl beta-D-maltoside in a pharmaceutical composition that otherwise includes diazepam, one or more tocopherols/tocotrienols, and benzyl alcohol as claimed.

Lastly, Patent Owner argues that the Patent Office determined the ’558 Provisional provided written description support for similar claims during the prosecution of a related patent. Prelim. Resp. 27, 33 (citing Ex. 1004, 28). During prosecution of the ’414 patent, the Examiner stated that “[t]he provisional Application incorporates a listing of n-dodecyl β-D-maltoside by reference to a Sigma Catalog” and concluded that the “claims receive a priority date of March 28, 2008.” Ex. 1004, 28. The Examiner provided no substantive analysis, however, on *why* that listing was sufficient to provide written description for the claims, nor did the Examiner grapple

with the argument and evidence now presented by Petitioner on this issue. *Id.* at 27–29.¹⁷ Accordingly, on this preliminary record, we reject any suggestion that the issue previously was resolved by the Office in a manner that warrants deference in this proceeding.

5. *Conclusion on Priority/Gwozdz’s Prior-Art Status*

At this time, we determine that the challenged claims are not entitled to priority to the filing date of the ’558 Provisional and, thus, the priority date for those claims is no earlier than March 27, 2009. Except as discussed below (Section III.F.2), Gwozdz is prior art as of the March 28, 2008, filing date of the Gwozdz Provisional.

F. *Obviousness over Gwozdz and Meezan (Ground 1)*

Petitioner argues that claims 1–25 would have been obvious over the combination of Gwozdz and Meezan. Pet. 26–61. The discussion below focuses on Petitioner’s challenge to independent claim 1.¹⁸

1. *Claim 1*

Petitioner argues the combination of Gwozdz and Meezan teaches the pharmaceutical solution of claim 1. Petitioner contends that Gwozdz teaches most of claim 1’s limitations, and Meezan teaches the addition of an alkyl

¹⁷ Insofar as some of Petitioner’s priority arguments resemble arguments raised in the 451 IPR, the Examiner briefly acknowledged the 451 IPR (Ex. 1004, 29) but never substantively addresses those arguments or the Board’s decision to explain what may reasonably be interpreted as an inconsistency between the Examiner’s and Board’s priority determinations. *See* Paper 12, 3 (Director referral decision citing an apparent contradiction between priority determinations as raising concerns of material error).

¹⁸ Patent Owner does not argue the patentability of the challenged claims separately. Prelim. Resp. 33–40 (arguing, for all claims, that Petitioner relies on certain non-prior art evidence to support the POSA’s asserted motivation for combining Gwozdz and Meezan).

glycoside, including n-dodecyl beta-D-maltoside, for use in intranasal formulations. Pet. 35–41. We summarize Petitioner’s argument below.

According to Petitioner, Gwozdz teaches pharmaceutical solutions for intranasal administration as recited in claim 1’s preamble (if limiting). *Id.* at 35–36 (citing, e.g., Ex. 1009, 4:24–26, 9:19–10:2; Ex. 1062 ¶¶ 128–132). Petitioner further argues that Gwozdz discloses “a therapeutically effective amount of diazepam” as recited in claim 1. *Id.* at 37 (citing, e.g., Ex. 1009, 8:6–18 (disclosing therapeutic agents include “benzodiazepines such as Diazepam”). Dr. Donovan also cites Meezan’s disclosure of intranasal drug formulations and opines that a POSA would have understood Meezan’s teachings as applicable to small-molecule drug compounds like diazepam. Ex. 1062 ¶¶ 130, 134; Ex. 1010 ¶¶ 8, 49; Pet. 36–37.

Petitioner contends that Gwozdz teaches the addition of tocopherols and alcohols (including benzyl alcohol) in amounts that overlap with those components of the pharmaceutical solution as recited in claim 1. Pet. 38–40 (citing, e.g., Ex. 1009, 4:17–21, 5:12–14, 5:33–6:2, 6:13–19, 7:8–11, 7:20–25). Dr. Donovan testifies there is no “criticality” associated with the claimed amounts of tocopherols and alcohols and the amounts of those components would have been subject to routine experimentation and optimization by the POSA. Ex. 1062 ¶¶ 141–145.

Lastly, Petitioner argues that Meezan describes absorption-enhancing compounds and, specifically, a use of “alkyl glycosides, including dodecyl maltoside.” Pet. 40–41 (citing, e.g., Ex. 1010 ¶¶ 56, 58, 61 (listing dodecyl maltoside as a preferred alkyl glycoside), 150–151, 158–159, Table 1 (dodecyl maltoside exemplified for ocular formulations); Ex. 1062 ¶¶ 147–153; *see also id.* ¶ 151 n.3 (testifying “[t]he terms dodecyl maltoside and ‘n-

dodecyl beta-D-maltoside’ are understood to be the same compound, and the terms are generally interchangeable”).

Patent Owner does not at this time contest that the combination of Gwozdz and Meezan discloses all the limitations of claim 1 (or the other challenged claims). Petitioner’s un rebutted argument and evidence supports a finding that Petitioner is reasonably likely to prevail in showing at trial that Gwozdz and Meezan together teach or suggest all the limitations of claim 1’s pharmaceutical solution.

2. *Motivation to Combine and Reasonable Expectation of Success*

Petitioner contends that, based on the teachings of the prior art and background knowledge, a POSA would have been motivated to combine Gwozdz and Meezan with a reasonable expectation of success. Pet. 27–35. Petitioner asserts, *inter alia*, that it was well known that benzodiazepine drugs (e.g., diazepam) can be difficult to administer due to the drugs’ limited solubility. *Id.* at 27–28 (citing Ex. 1001, 1:45–49; Ex. 1062 ¶¶ 101–102). Gwozdz, Petitioner explains, teaches one approach to improve the solubility of benzodiazepines and, thus, drug delivery to nasal membranes, which involves dissolving difficult-to-solubilize therapeutic agents in solvents containing, for example, tocopherols and alcohols. *Id.* at 28 (citing Ex. 1009 7:29–34, 9:19–22). Petitioner contends that Gwozdz teaches other additives may also be included to improve efficacy. *Id.* at 29 (citing Ex. 10:12–16; Ex. 1062 ¶ 104).

Petitioner also cites Meezan’s teaching of drug-enhancing agents useful for increasing the absorption and bioavailability of drugs delivered via, for example, the nasal route. *Id.* (citing Ex. 1010 ¶ 4). According to Petitioner, while Gwozdz focused on improving solubility using tocopherol- and alcohol-based solvent systems, “Meezan presented an additional and

unique formulation strategy to increase absorption and bioavailability” by using alkyl glycosides as absorption-enhancing compounds—motivating a POSA to add an alkyl glycoside, including n-dodecyl beta-D-maltoside, in the pharmaceutical solutions of Gwozdz and, thus, arriving at the subject matter of claim 1. *Id.* at 29–30 (citing, e.g., Ex. 1062 ¶¶ 104–105); *see also id.* at 31–33 (citing Meezan’s suggestion of utility to increase bioavailability of small molecule drugs (< 1.5 kDa), diazepam’s weight of 284.74 Daltons, and Meezan’s teaching of compatibility with alcohol-based solvent systems as further motivating the combination); Ex. 1010 ¶¶ 74, 130; Ex. 1017, 2677; Ex. 1062 ¶¶ 107–112. Indeed, Dr. Donovan testifies a POSA, “[i]n an effort to optimize the bioavailability of Gwozdz’s formulation . . . , would look to Meezan for guidance” and “[b]ased on Meezan’s teachings . . . would be motivated to add an alkyl glycoside to Gwozdz’s solution, with an expectation of successfully increasing the permeation and resulting bioavailability.” Ex. 1062 ¶¶ 147–152.

Patent Owner counters that, because Petitioner relies in its motivation-to-combine analysis on a “single statement” in Gwozdz that is *not prior art*, the motivation for combining Gwozdz and Meezan is defective and institution should be denied. Prelim. Resp. 33–39. More specifically, Patent Owner argues the Gwozdz Provisional’s listing of optional additives has a key omission compared to the corresponding listing in Gwozdz cited by Petitioner. *Id.* at 37. Patent Owner points out that Gwozdz lists “penetration enhancers” among its additives but that phrase is missing in the Gwozdz Provisional and, thus, Gwozdz’s mention of “penetration enhancers” is not

prior art.¹⁹ *Id.* at 37–39 (comparing Ex. 1009, 10:9–16, with Ex. 1064, 10:10–17). According to Patent Owner, because this missing phrase “provides the sole support the Petition advances for a motivation to combine,” the rationale for combining Gwozdz and Meezan fails. *Id.*

We agree with parts of Patent Owner’s argument but, on this preliminary record, not the conclusion Patent Owner asks us to reach.

We agree that at least one portion of Gwozdz is not prior art. To establish that the cited disclosures in Gwozdz are prior art, Petitioner must show support for those disclosures in the Gwozdz Provisional. *In re Riggs*, 131 F.4th 1377, 1384 (Fed. Cir. 2025) (explaining that “the portion of the application relied on . . . as prior art must be supported by the provisional application”). 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. 37.²⁰ Based on this record, we determine that Gwozdz’s mention of “penetration enhancers” is not prior art to the

¹⁹ Patent Owner argues this “penetration enhancers” disclosure in Gwozdz is not prior art regardless which of the disputed priority dates (March 28, 2008, or March 27, 2009) one accords to the challenged claims. Prelim. Resp. 33.

²⁰ We also agree that collateral estoppel does not bar Patent Owner from challenging Gwozdz’s prior-art status in this case. Patent Owner’s apparent concession that Gwozdz was prior art during the 451 IPR does not equate to the issue being actually litigated. Prelim. Resp. 34–35; Ex. 1040, 14 (“Patent Owner does not contest that Gwozdz is entitled to this filing date” of the Gwozdz Provisional). *Purdue*, 767 F. App’x at 922 (determining “[t]he priority date for the Joshi reference . . . cannot be determined based on collateral estoppel” where patentee could have argued, but did not in fact argue, Joshi’s prior-art status in an earlier matter).

challenged claims. The phrase cannot, therefore, be used to establish a motivation to combine the asserted references.

We disagree, however, that Gwozdz’s non-prior art mention of penetration enhancers is the “sole support” provided by Petitioner for combining Gwozdz and Meezan to arrive at the claimed subject matter. Prelim. Resp. 39–40; *see also id.* at 33 (“Petitioner relies solely on a disclosure in Gwozdz . . . concerning ‘penetration enhancers’ to argue that a skilled artisan would have been motivated to combine Gwozdz with Meezan.”). To the contrary, Petitioner provides additional reasoning that does not appear to turn on Gwozdz’s disclosure of “penetration enhancers” among a list of additives. Petitioner cites, *inter alia*, known solubility issues with diazepam limiting delivery of sufficient drug to the tissues desired, Meezan’s teachings about increasing bioavailability of drugs meant for nasal administration by the addition of absorption-enhancing alkyl glycosides, and Meezan’s suggestion that its formulations are compatible with non-aqueous solvent systems (such as Gwozdz’s solvents for intranasal delivery) and suitable for use with small-molecule drugs (like diazepam). *See, e.g.*, Pet. 27–33. We recognize Dr. Donovan’s (and by extension Petitioner’s) reference to Gwozdz’s listing of “penetration enhancers” in support of the asserted motivation to combine. *See, e.g.*, Ex. 1062 ¶¶ 104, 109, 149. But, for reasons noted above, Patent Owner may be overstating the extent and criticality of Petitioner’s reliance on this non-prior-art evidence, which we determine is best judged on a fully-developed record.

Finally, as it relates to the motivation to combine Gwozdz and Meezan, Petitioner also argues that collateral estoppel applies. Pet. 8–10. The motivation to combine Gwozdz and Meezan was litigated at length and decided in the 451 IPR. *See, e.g.*, Ex. 1040, 37–47 (finding, *inter alia*, “a

person of ordinary skill in the art would have had reason to add alkyl glycoside as a penetration enhancer, as disclosed in Meezan '962, with a formulation of benzodiazepine, tocopherol, ethanol, and benzyl alcohol, as disclosed in Gwozdz"). And, although we appreciate that the language of the challenged claims in the two proceedings is not identical (e.g., an "alkyl glycoside" was a component of claim 1 in the 451 IPR, while the specific alkyl glycoside in claim 1 here is "n-dodecyl beta-D-maltoside"), we do not see at present how those differences materially alter the motivation-to-combine issue.

If the POSA would have been motivated to add an alkyl glycoside, as disclosed in Meezan, to the pharmaceutical solution of Gwozdz—an issue Patent Owner already litigated and lost—Patent Owner should be prepared to explain at trial why a POSA's selection of a preferred alkyl glycoside in Meezan (i.e., dodecyl maltoside) raises a materially distinct question of patentability.²¹ *Ohio Willow Wood*, 735 F.3d at 1342–43 (applying collateral estoppel where patentee did not explain how a difference in claim language was "patentably significant in view of the obviousness determination" of similar claims in a related patent); *Google*, 54 F.4th at 1381–82 (applying collateral estoppel where differences in adjudicated and

²¹ In the 451 IPR and for those dependent claims reciting "dodecyl maltoside," the Board credited argument that Meezan taught dodecyl maltoside as a "preferred alkyl glycoside." See Ex. 1040, 33–37 (citing, e.g., Meezan (Ex. 1011 in the 451 IPR; Ex. 1010 here)) ¶¶ 56, , 58, 61, 92, 150, 151, 155–158, 167, Table I, Fig. 1). There is no dispute at present that dodecyl maltoside is indeed a preferred alkyl glycoside in Meezan. See, e.g., Ex. 1010 ¶¶ 58 (dodecyl maltoside listed among "preferred glycosides"), 156–159 (identifying "dodecyl-β-D-maltoside" as preferred; "dodecyl-, tridecyl- and tetradecyl-β-D-maltosides, are more effective").

unadjudicated claims were minor and did not “materially alter the question of patentability [(i.e., obviousness)]”).

3. Conclusion

For the reasons discussed above and based on the present record, we find that Petitioner has made an adequate threshold showing that the combination of Gwozdz and Meezan discloses the pharmaceutical solution of claim 1 and that a skilled artisan would have combined those references with a reasonable expectation of success. We therefore determine that Petitioner has shown that it is reasonably likely to prevail in establishing that at least claim 1 would have been obvious over Gwozdz and Meezan.

G. Obviousness over Gwozdz, Meezan, and Cartt (Ground 2) and Gwozdz, Meezan, and USP 23/NF 18 (Ground 3)

Petitioner argues that dependent claims 20 and 21 would have been obvious over the combinations of Gwozdz, Meezan, and Cartt (Ground 2), and that dependent claims 26 and 27 would have been obvious over Gwozdz, Meezan, and USP 23/NF 18. Pet. 61–66.

Petitioner supports its challenge under Grounds 2 and 3 with citation to the teachings of the asserted prior art and the testimony of its declarant, Dr. Donovan. *Id.* (citing, e.g., Ex. 1065 ¶¶ 28, 63–63; Ex. 1066, 1631; Ex. 1062 ¶¶ 120–121, 251–258, 261–266). Patent Owner raises no counterargument beyond that already addressed above under Ground 1.

Considering the evidence and argument at this stage, we determine that Petitioner is reasonably likely to prevail in showing the unpatentability of one of more of the claims challenged under Grounds 2 and 3.

IV. CONCLUSION

Petitioner has shown a reasonable likelihood that it will prevail in establishing the unpatentability of at least one of the claims challenged in the

Petition. We institute trial on all challenged claims under the grounds raised in the Petition. *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (explaining that institution of *inter partes* review “require[s] a simple yes-or-no institution choice . . . embracing all challenges included in the petition”); 37 C.F.R. § 42.108(a).

Any argument not raised in a Patent Owner Response to the Petition, or as permitted in another manner during trial, shall be deemed forfeited and/or waived even if asserted in the Preliminary Response. *In re Google Tech. Holdings LLC*, 980 F.3d 858, 862–64 (Fed. Cir. 2020) (holding an argument forfeited when not timely raised before the Board); *In re NuVasive, Inc.*, 842 F.3d 1376, 1380–81 (Fed. Cir. 2016) (holding Patent Owner waived an argument addressed in the Preliminary Response by not raising the same argument in the Patent Owner Response).

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review of all challenged claims of the ’786 patent is instituted on the grounds of unpatentability set forth in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(a) and 37 C.F.R. § 42.4, notice is given of institution of trial commencing on the entry date of this Decision.

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