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Paper 91
Entered: May 7, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

MERCK SHARP & DOHME CORP.,
Patent Owner.

IPR2020-00040[1]
Patent 7,326,708 B2

Before SHERIDAN K. SNEDDEN, ROBERT A. POLLOCK, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

MAJORS, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining No Challenged Claims Unpatentable
35 U.S.C. § 318(a)
Denying Patent Owner's Motion to Exclude
37 C.F.R. § 42.64

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[1] Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. were joined as parties to this proceeding via Motion for Joinder in IPR2020-01060; and Sun Pharmaceuticals Industries Ltd. was joined as a party to this proceeding via Motion for Joinder in IPR2020-01072.

I. INTRODUCTION

Mylan Pharmaceuticals Inc. ("Petitioner" or "Mylan"),[2] on October 30, 2019, filed a Petition to institute *inter partes* review of claims 1–4, 17, 19, and 21–23 of U.S. Patent No. 7,326,708 B2 (Ex. 1001, "the '708 patent"). Paper 1 ("Pet." or "Petition"). On May 12, 2020, based on the preliminary record, we instituted *inter partes* review of the challenged claims on all asserted grounds. Paper 21 ("Inst. Dec.").

After institution, Patent Owner Merck Sharp & Dohme Corp. ("Patent Owner" or "Merck") filed a Response. Paper 41 ("PO Resp."). Petitioner filed a Reply. Paper 65 ("Reply"). Patent Owner filed a Sur-reply. Paper 74 ("Sur-reply"). Also before us is Patent Owner's Motion to Exclude (*see* Papers 81, 85). We held an oral hearing on February 11, 2021, and the transcript is on file. Paper 90 ("Tr.").

As a brief overview, the claims here relate to a compound called "sitagliptin" and, specifically, to particular dihydrogenphosphate ("DHP") salt forms of it that have a 1-to-1 ratio, or stoichiometry, between the relevant phosphate anion and the corresponding sitagliptin cation. Pet. 1–2; PO Resp. 1 (discussing "1:1 sitagliptin DHP"); Ex. 1001, 2:44–65, 15:64–16:15 (claim 1). Sitagliptin is among a class of compounds known as dipeptidyl peptidase-IV inhibitors, which can inhibit an enzyme implicated in the etiology of non-insulin dependent diabetes mellitus (i.e., Type 2 diabetes). *Id.* at 1:3–36. Indeed, Merck developed and sells its drug

[2] Petitioner identifies itself, Mylan Inc., and Mylan N.V. as the real parties-in-interest. Pet. 6.

product, Januvia, which is indicated for treatment of Type 2 diabetes and includes a 1:1 sitagliptin DHP salt. PO Resp. 1, 25–26; Ex. 2003 ¶ 2.[3]

The dispute in this case focuses, in large part, on whether an earlier-filed international patent application, which Merck also owns, expressly or inherently discloses the 1:1 sitagliptin DHP salt claimed in the '708 patent.[4] At institution, and despite our determination that this prior art included no explicit disclosure of a phosphate salt of sitagliptin having the 1:1 stoichiometry, we nevertheless instituted trial based, *inter alia*, on testimony from Petitioner's expert that sitagliptin can only be mono-protonated and reacting sitagliptin with phosphoric acid forms the 1:1 DHP salt "every time" and is, thus, inherent. Inst. Dec. 52–53 (noting preliminary record "suggest[s] the 1:1 salt is the necessary byproduct of contacting phosphoric acid and sitagliptin"). Because it is undisputed that the prior art does not expressly disclose the specific 1:1 DHP salt of sitagliptin,[5] and the evidence through trial now shows that sitagliptin can form phosphate salts in non-1:1 ratios without necessarily forming the 1:1 salt (i.e., no inherency), Merck argues that Petitioner's anticipation challenge fails. PO Resp. 6–19.

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[3] Merck has indicated that "the crystalline monohydrate form of the DHP salt . . . is the solid form of sitagliptin used today in Merck's products." Paper 10, 4–5.

[4] The published international patent application (WO 03/004498) and a U.S. counterpart patent (US 6,699,871; also asserted here as anticipating art) contain materially "identical" disclosures. *See* Pet. 33; Tr. 7:8–13.

[5] *See* Tr. 15:7–19 (Petitioner's counsel agreeing that "there's no express disclosure of a 1:1 DHP salt of sitagliptin in the WO ['498] reference or the '871 reference"); Ex. 2103 ¶ 67.

If anticipation fails, Petitioner is left with obviousness. But, in Merck's telling, the obviousness challenge fares no better because Merck's inventors reduced to practice the subject matter of almost all the challenged claims before the key prior art published, thus disqualifying that art as a § 102(a) reference; and, even if that art still qualifies under § 102(e), Merck's common ownership of the art eliminates it from the obviousness analysis under § 103(c)(1).[6] PO Resp. 22–28. For the two dependent claims for which Merck does not argue an earlier reduction to practice, Merck contends those claims are not obvious because, among other things, that claimed subject matter was highly unpredictable and Petitioner failed to show a reason why it would have been made by an ordinarily skilled person with a reasonable expectation of success. *Id.* at 38–59.

We address in detail the parties' arguments on anticipation and obviousness in the sections below. On this trial record, however, we find Petitioner has failed to show by a preponderance of the evidence that claims 1–4, 17, 19, and 21–21 are unpatentable. Petitioner has, thus, not met its burden and proved unpatentability of the challenged claims. 35 U.S.C. § 316(e). Our reasoning is detailed in Section II below.

We also deny Patent Owner's Motion to Exclude. *Infra* Section III.

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[6] Under the pre-AIA § 103(c)(1) exception, subject matter developed by "another person" that qualifies as prior art under § 102(e) can be eliminated from use in an obviousness analysis if that subject matter and the claimed invention are commonly owned or under obligation of assignment to the same person or entity at the time of the invention. 35 U.S.C. § 103(c)(1).

A. Related Patents and Proceedings

"[T]here are no related United States patents or pending applications" and "this is the first IPR directed to the '708 patent." Pet. 7, 67.

Petitioner identifies several related cases before the courts including, without limitation: *Merck Sharp & Dohme Corp. v. Mylan Pharm. Inc. et al.*, 1:19:-cv-00101 (N.D. W. Va.); *Merck Sharp & Dohme Corp. v. Mylan Pharm. Inc. et al.*, 1:19-cv-01489 (D. Del.); and *Merck Sharp & Dohme Corp. v. Sandoz, Inc.*, 1:19-cv-00312 (D. Del.). Pet. 6–7 (listing cases). Patent Owner states that it "filed Hatch-Waxman suits alleging infringement of the '708 patent, among others, against fourteen generic drug companies including Mylan, Teva, Apotex, Par, Sun, and Sandoz." Paper 10, 10. The litigation against the generic drug companies "has been consolidated for pretrial proceedings in a multidistrict litigation ('MDL')" before the district court in Delaware. *Id.* (identifying *In re Sitagliptin Phosphate ('708 & '921) Patent Litig.*, C.A. No. 19-md-2902-RGA (D. Del.)).

There are also related matters filed with the Board. After institution, other petitioners filed substantially identical petitions challenging claims of the '708 patent and requested joinder with Mylan in this proceeding. *See* IPR2020-01045 ("Teva" matter); IPR2020-01060 ("Dr. Reddy's" matter); IPR2020-01072 ("Sun" matter). We instituted trial in those other matters and joined the petitioners as parties here. IPR2020-00040, Papers 44–46. The Dr. Reddy's and Sun parties remain joined. The Teva parties (Teva Pharmaceuticals USA, Inc. and Watson Laboratories, Inc.) have settled with Merck and IPR2020-01045 is terminated. IPR2020-01045, Paper 25. The Teva parties are no longer joined. IPR2020-00040, Paper 73, 2–3.

B. Asserted Grounds of Unpatentability

Petitioner asserts six grounds of unpatentability (Pet. 12) as set forth in the table below:

Claim(s) Challenged	35 U.S.C. §	Basis
1–3, 17, 19, 21–23	102(a), 102(e)(2)[7]	WO '498[8]
1–3, 17, 19, 21–23	102(e)(2)	'871 patent[9]
3, 17, 19, 21–23	103	WO '498
1–3, 17, 19, 21–23	103	WO '498, Bastin[10]
4	103	WO '498, Bastin, Brittain[11]
4	103	WO '498, Brittain

[7] The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) ("AIA"), amended 35 U.S.C. §§ 102 and 103. The '708 patent's claims have an effective filing date before the effective date of those amendments so we refer to the pre-AIA versions of §§ 102 and 103 here.
[8] Edmondson et al., WO 03/004498 A1, published Jan. 16, 2003 (Ex. 1004, "WO '498"). WO '498 published from Application No. PCT/US02/21349, filed July 5, 2002, which claims priority to US Provisional Application No. 60/303,474, filed July 6, 2001 (Ex. 1012).
[9] Edmondson et al., US 6,699,871 B2, issued Mar. 2, 2004 (Ex. 1007, "the '871 patent"). The '871 patent issued from an application filed July 5, 2002, and claims priority to US Provisional Application No. 60/303,474, filed July 6, 2001 (Ex. 1012).
[10] Richard J. Bastin et al., *Salt Selection and Optimisation Procedures for Pharmaceutical New Chemical Entities*, 4 ORGANIC PROCESS RESEARCH & DEVELOPMENT 427–435, 2000 (Ex. 1006, "Bastin").
[11] Polymorphism in Pharmaceutical Solids, Harry G. Brittain ed., 1999 (Ex. 1005, "Brittain").

Petitioner relies on the Declaration of Mukund Chorghade, Ph.D. (Ex. 1002) and Dr. Chorghade's Reply Declaration (Ex. 1035), among other evidence.

Patent Owner relies on the Declaration of Allan S. Myerson, Ph.D. (Ex. 2101), the Declaration of Adam J. Matzger, Ph.D. (Ex. 2103), and testimony from several current or former Merck employees (including many of the '708 patent's eight named inventors), among other evidence. *See, e.g.*, Exs. 2002 (Vydra Decl.), 2003 (Wenslow Decl.), 2004 (Ferlita Decl.), 2005 (Diddle Decl.), 2109 (Herman Decl.), 2124 (Cypes Decl.), 2127 (Hansen Decl.), and 2140 (Shultz Decl.).

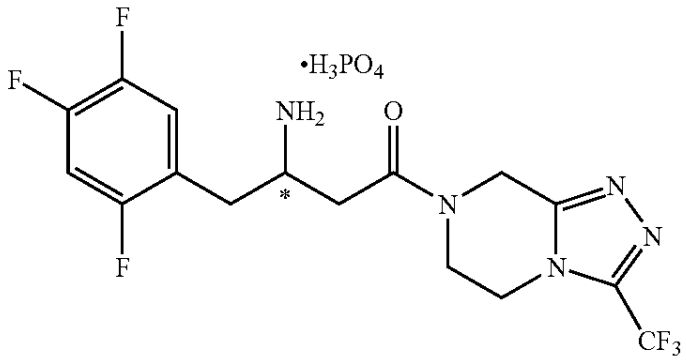
C. The '708 Patent

The '708 patent is titled "PHOSPHORIC ACID SALT OF A DIPEPTIDYL PEPTIDASE-IV INHIBITOR." Ex. 1001, code (54). The '708 patent claims priority to non-provisional and provisional patent applications filed, respectively, on June 23, 2004, and June 24, 2003. *Id.* at codes (21), (22), (60). The patent issued February 5, 2008. *Id.* at code (45).

According to the '708 patent, "[t]he present invention relates to a particular salt of a dipeptidyl peptidase-IV inhibitor," and specifically, the dihydrogenphosphate ("DHP") salt of 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine. *Id.* at 1:13–17. The chemical,4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine, is also known as "sitagliptin." *See*

Ex. 2003 ¶ 2; Pet. 1 n.1.[12] The structural formula for the DHP salt of sitagliptin is shown below as formula (I):

(I)



Ex. 1001, 2:44–63. This formula reflects a salt with one phosphate anion associated with one sitagliptin amine cation (with a stereogenic carbon at *). *Id.* at 3:46–52 ("[T]he dihydrogenphosphate salt of the present invention is comprised of one molar equivalent of mono-protonated [sitagliptin] . . . and one molar equivalent of the dihydrogenphosphate (biphosphate) anion.").

The '708 patent states that this salt is "useful for the treatment and prevention of diseases and conditions for which an inhibitor of dipeptidyl peptidase-IV is indicated, in particular Type 2 diabetes." *Id.* at 1:19–22.

In a section related to background of the invention, the '708 patent identifies WO 03/004498 (i.e., WO '498), which is "assigned to Merck &

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[12] Petitioner notes, without dispute, that sitagliptin is also the compound with the chemical name: 7-[(3R)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-α]pyrazine. Pet. 1 n.1; Ex. 1004, 47 (Example 7). In citing asserted references and technical publications in this Decision, we generally use the page numbers added to the exhibit not the original pagination, except that, for US patents, we use the column and line number format or other indicia.

Co." *Id.* at 1:49–50. The '708 patent states that WO '498 "describes a class of beta-amino tetrahydrotriazolo[4,3-a]pyrazines, which are potent inhibitors of DP-IV and therefore useful for the treatment of Type 2 diabetes." *Id.* at 1:50–52. According to the '708 patent, WO '498 "[s]pecifically disclose[s]" the 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazine-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine. *Id.* at 1:53–55. The patent states that "[p]harmaceutically acceptable salts of this compound are generically encompassed within the scope of WO 03/004498." *Id.* at 1:53–57. "However," the '708 patent states, "there is no specific disclosure in the above reference [(WO '498)] of the newly discovered monobasic dihydrogenphosphate salt . . . of structural formula I." *Id.* at 1:58–62.

The '708 patent further notes the following about WO '498:

> The crystalline dihydrogenphosphate salt of the present invention exhibits pharmaceutic advantages over the free base and the previously disclosed hydrochloride salt (WO 03/004498) in the preparation of a pharmaceutical drug product containing the pharmaceutically active ingredient. In particular, the enhanced chemical and physical stability of the crystalline dihydrogenphosphate salt monohydrate constitute advantageous properties in the preparation of solid pharmaceutical dosage forms containing the pharmacologically active ingredient.

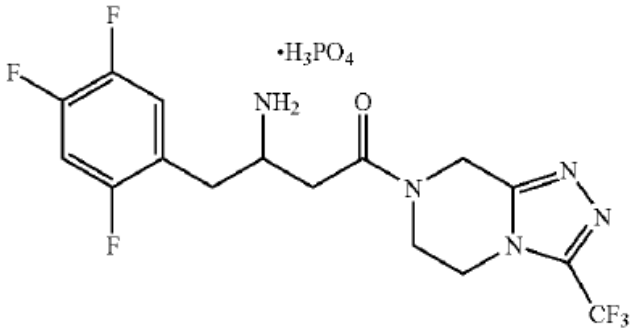
Id. at 4:19–28.

D. Challenged Claims

The '708 patent includes twenty-four claims. Petitioner challenges claims 1–4, 17, 19, and 21–23. Claims 1, 2, and 4 are illustrative and read as follows:

1. A dihydrogenphosphate salt of 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazine-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine of structural formula I:

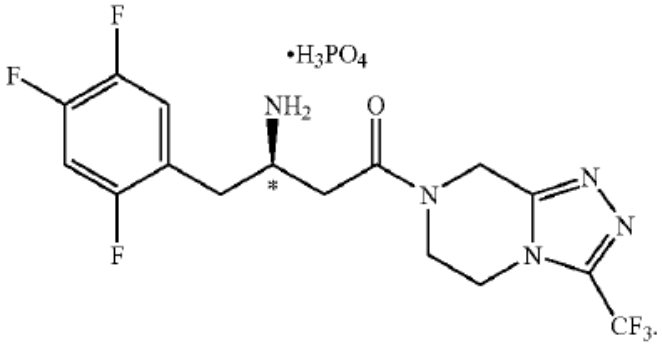
(I)



or a hydrate thereof.

2. The salt of claim 1 of structural formula II having the (R)-configuration at the chiral center marked with an *

(II)



4. The salt of claim 2 characterized as being a crystalline monohydrate.

Ex. 1001, 15:64–16:30, 16:48–49. Each of the other challenged claims depends (directly or indirectly) on claims 1 or 2. *See, e.g., id.* at 17:29–32 (claim 19: method of treating type 2 diabetes with the salt of claim 2), 17:37–18:5 (claim 21: process for preparing the salt of claim 2).

II. ANALYSIS

A. Principles of Law

"In an IPR, 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)).

To show anticipation under 35 U.S.C. § 102, each and every claim element, arranged as in the claim, must be found in a single prior art reference. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359 (Fed. Cir. 2008). The prior art need not, however, use the same words as the claims. *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009). The anticipation inquiry takes into account the literal teachings of the prior art reference, and inferences the ordinarily skilled person would draw from it. *Eli Lilly and Co. v. Los Angeles Biomedical Res. Inst. at Harbor-UCLA Med. Ctr.*, 849 F.3d 1073, 1074–75 (Fed. Cir. 2017). Indeed, "a reference can anticipate a claim even if it does not expressly spell out all the limitations arranged or combined as in the claim, if a person of skill in the art, reading the reference, would at once envisage the claimed arrangement or combination." *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015) (internal quotation marks omitted).

As to obviousness, a claim is unpatentable under 35 U.S.C. § 103 if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the 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) objective evidence of nonobviousness when presented. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). A party who petitions the Board for a determination of unpatentability based on obviousness must show 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." *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016) (quotations and citations omitted).

B. Person of Ordinary Skill in the Art

In determining the level of skill in the art, we consider the problems encountered in the art, the art's solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the educational level of active workers in the field. *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986).

Petitioner contends a person of ordinary skill in the art (or "POSA") at the time of the invention would have had:

> (i) a Ph.D. in chemistry, biochemistry, medical chemistry, pharmacy, pharmaceutics, or a related field, and at least two years of relevant experience in drug development including an understanding of salt selection in drug development; (ii) a master's degree in the same fields and at least five years of the same relevant experience; or (iii) a bachelor's degree in the same fields and at least seven years of the same relevant experience.

Pet. 11; Ex. 1002 ¶¶ 45–46. Patent Owner does not oppose this definition.[13]

We find Petitioner's proposed definition is consistent generally with the cited prior art, and we apply it for the purposes of this Decision. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown") (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985)).

C. Claim Construction

We interpret a claim "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b)." 37 C.F.R. § 42.100(b) (2019). Under this standard, we construe the claim "in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *Id.* "[W]e need only construe terms 'that are in controversy, and only to the extent necessary to resolve the controversy.'" *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*

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[13] Merck's experts, Drs. Myerson and Matzger, phrase the definition differently—limiting the fields of study to "chemistry, chemical engineering or a related field," and requiring two or more years (depending degree attained) "working with pharmaceutical solids, including polymorphic forms." Ex. 2101 ¶ 39; Ex. 2103 ¶ 40. Neither party contends, however, that any disputed matter turns on acceptance of one definition or the other. Merck's experts state that their opinions do not change under either definition. Ex. 2101 ¶ 40; Ex. 2103 ¶ 41.

Ltd., 868 F.3d 1013, 1017 (Fed. Cir. 2017) (quoting *Vivid Tech., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

At institution, neither party requested any express claim construction. Pet. 10 ("Petitioner submits that no further construction [beyond the claims as written] is necessary"); Ex. 1002 ¶¶ 57–59.

Claim 21 is a dependent claim and recites a process for preparing the 1:1 (R)-sitagliptin DHP of claim 2. Ex. 1001, 17:37–18:5. Petitioner, in its Reply, argues that claim 21's "contacting" limitation "means an actual physical interaction between molecules." Reply at 11–12. Petitioner's position is that the claim phrase "contacting one equivalent of [sitagliptin] in an organic solvent or aqueous organic solvent with about one equivalent of phosphoric acid at a temperature in the range of about 25–100°C" does not limit the molar amounts of the acidic and basic reagents provided in the solvent, but rather how discrete molecules actually interact to form the final salt. *Id.*; Ex. 1001, 17:38–18:5; Tr. 23:23–25:9. In Petitioner's view, "the sitagliptin base molecule is *only able* to interact once with a phosphoric acid molecule." Reply 12. And because a 1:1 salt allegedly always forms when an acid (e.g., hydrochloric or phosphoric) is reacted with sitagliptin, the "contacting" step would be met even if the reaction conditions were to include using a large excess (i.e., a substantially non-equivalent molar amount) of acid molecules relative to the base, such as the excess hydrochloric acid in WO '498's Example 7.[14] Reply 12–13.

[14] Put differently, Petitioner's position is that it does not matter what molar amounts of the acid and base are used (e.g., 100 moles of acid vs. 1 mole of

Patent Owner responds that Petitioner is abrogating claim 21's limitations. According to Patent Owner, Petitioner's interpretation and application of the art to claim 21 renders irrelevant: (i) the starting materials (insofar as the cited art starts with BOC-protected sitagliptin, not sitagliptin free base); and (ii) the claim's "one equivalent" language (insofar as the cited example in the art uses a substantial molar excess of the acid), so long as a salt with 1:1 stoichiometry might somewhere form in a downstream process. Sur-reply 13–14; *see also* Ex. 2103 ¶ 232 (describing WO '498's Example 7 as "using ~1000 fold excess of hydrochloric acid").

Given the present record, we are unpersuaded that a further construction of claim 21 is required. Even if we agreed with Petitioner's interpretation, Petitioner has not proved that the cited art expressly or inherently discloses preparing the 1:1 DHP salt of sitagliptin (discussed *infra* for anticipation challenges). Alternatively, if claim 21 required use of one molar equivalent of sitagliptin and about (i.e., "approximately") one molar

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base would still be encompassed); key to Petitioner's argument is the final result of a 1:1 salt, thus allegedly proving the reagents will only interact in a 1:1 ratio. We explained at the oral hearing that we found Petitioner's interpretation problematic because it cited no intrinsic evidence in support and also appeared to read the term "about" out of the claim. Tr. 25:2–27:6 (asking how it's possible to have interaction at a molecular level as suggested by Petitioner (seemingly requiring whole numbers ratios, like 1:1 or 1:2, in which the molecules might interact and bond) between one equivalent of a molecule and *about* one equivalent of another). Petitioner had no satisfactory response to those concerns. *Id.*; *see also id.* at 75:14–21 (Petitioner's counsel later suggested that even if the "contacting" step required use of equal molar amounts, using such amounts would be an obvious change "that you would indeed use").

equivalent of acid in the solvent (*see* Ex. 1001, 6:29–55 (disclosing a process for preparing the claimed 1:1 sitagliptin DHP)), Petitioner has not shown that WO '498 describes that reaction. Again, it is undisputed that the cited example (Example 7 of WO '498) uses a substantial molar excess of the acid (HCl) to the base. On obviousness and as explained below (*see* Section II(F)), we conclude that Patent Owner's reduction-to-practice evidence is dispositive for several claims, including claim 21, and that issue does not turn on whether we accept or reject Petitioner's interpretation (which encompasses, but is not limited to, using equimolar amounts). PO Resp. 25 (explaining, citing undisputed evidence, how the inventors made 1:1 sitagliptin DHP with "equimolar" amounts of sitagliptin and phosphoric acid under conditions encompassed by claim 21).

D. Anticipation by WO '498

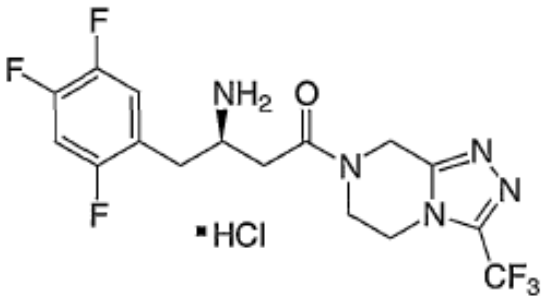
Petitioner asserts that claims 1–3, 17, 19, and 21–23 are unpatentable as anticipated by WO '498. Pet. 12–31. We provide an overview of WO '498, and then turn to analysis of the alleged anticipation.

1. Overview of WO '498 (Exhibit 1004)

WO '498 "is directed to compounds which are inhibitors of the dipeptidyl peptidase-IV enzyme ('DP-IV inhibitors') and which are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes." Ex. 1004, 1. WO '498 is further "directed to pharmaceutical compositions comprising these compounds and the use of these compounds and compositions" for treatment or prevention of the above-noted diseases. *Id.*

WO ’498 discloses several examples of the compounds of its invention. *Id.* at 38–47 (describing Examples 1–7); *see also id.* at 48–49 (identifying other example compounds, numbered examples 8–33). The salt of Example 7 is shown in the chemical structure below.

EXAMPLE 7



7-[(3*R*)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-*a*]pyrazine, hydrochloride

Id. at 47:1–5; *see also id.* at 47:6–26 (describing steps for preparing the compound and salt of Example 7). The structure in Example 7 of WO ’498 “depicts the hydrochloride salt of sitagliptin in its (R)-configuration.” Ex. 1002 ¶ 67.

WO ’498 does not describe or exemplify any specific phosphate salt of sitagliptin (or any phosphate of the other compounds). More generically, however, WO ’498 claims (R)-sitagliptin and several other compounds, and pharmaceutically acceptable salts thereof. WO ’498 claims:

15. A compound which is selected from the group consisting of:

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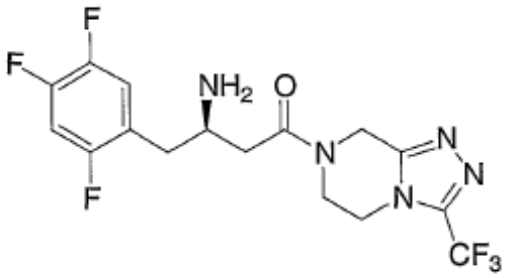

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and pharmaceutically acceptable salts thereof.

Ex. 1004, 55:16–61:5 (claim 15 depicts thirty-three DP-IV inhibitor compounds, one of which is (R)-sitagliptin (shown in the excerpt above), and, after depicting all those compounds, recites "and pharmaceutically acceptable salts thereof").

WO '498 elsewhere describes "'pharmaceutically acceptable salts' [as] refer[ring] to salts prepared from pharmaceutically acceptable non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids." *Id.* at 10:27–29. "When the compound of the present invention is basic," WO '498 indicates the "salts may be prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids," and WO '498 identifies twenty-six illustrative acids. *Id.* at 11:8–14 ("Such acids include acetic, benzenesulfonic, benzoic, . . . hydrochloric, . . . phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid, and the like."). Among the twenty-six acids named, WO '498 discloses that "[p]articularly preferred are citric, hydrobromic, hydrochloric, maleic, phosphoric, sulfuric, fumaric,

and tartaric acids." *Id.* at 11:14–15; *see also id.* at 11:16–17 ("It will be understood, as used herein, references to the compounds of Formula I are meant to also include the pharmaceutically acceptable salts.").

2. Analysis of Alleged Anticipation

a) The Parties' Arguments

Petitioner contends that WO '498 discloses (R)-sitagliptin and its pharmaceutically acceptable salts. Pet. 16–17 (citing Ex. 1004, 55–60 ("Claim 15 (7th compound)"). Petitioner further argues that WO '498's disclosure of acceptable salts would include at least the eight "[p]articularly preferred" acids, one of which is phosphoric acid, as a non-toxic acid for use in forming salts with compounds like sitagliptin. *Id.* at 16–18; *see* Ex. 1004, 10:8–15. Thus, Petitioner argues, "WO '498 teaches the phosphoric acid salt of sitagliptin" and a specific example is not needed. *Id.* at 16–18.

According to Petitioner, this case involves anticipation by disclosure of "lists," not necessarily anticipation where the art discloses a genus and a species within that genus are claimed. Pet. 20–22 (citing, *e.g.*, *Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1361 (Fed. Cir. 2012)); *see also id.* at 23–24 (citing *In re Gleave*, 560 F.3d 1331, 1331 (Fed. Cir. 2009) ("For purposes of whether they are anticipatory, lists and genera are often treated differently under our case law.")).[15] More specifically,

[15] Whether a disclosed genus anticipates a species ordinarily turns on whether the prior art "expressly spelled out a definite and limited class of compounds that enabled a person of ordinary skill in the art to at once envisage each member of this limited class." *Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1376 (Fed. Cir. 2006); *Atofina v.*

Petitioner contends "WO '498 provides two closed lists," where "[t]he primary list (i.e., Claim 15) provides 33 compounds" and the "secondary" list "identifies by name the eight" preferred acids. *Id.* at 22. Because the first list includes (R)-sitagliptin and the second list includes phosphoric acid, Petitioner contends "neither list leaves anything to the imagination" and WO '498 anticipates claims 1 and 2. *Id.* at 22–24. Petitioner asserts that WO '498's disclosures even arguably "collapse to form a single comprehensive list" of all the compounds and salts. *Id.* at 23–24; Ex. 1002 ¶ 80. And, because lists are involved, Petitioner argues "the number of [listed items] is irrelevant." *Id.* at 24 (citing *In re Gleave*, 560 F.3d at 1333, 1338 (explaining that the art "expressly lists every possible fifteen-base-long oligodeoxynucleotide sequence in IGFBP-2," and that the "list include[d] more than 1400 sequences")).

Petitioner does not, in the Petition, address the 1:1 stoichiometry limitation of the claimed salt head-on. To the extent addressed at all, Petitioner's discussion appears in parts of a footnote spanning several pages. Pet. 18–20 n.8. There, Petitioner states that claim 1's "dihydrogenphosphate salt" of sitagliptin, "is nothing more than another name for the (monobasic) phosphoric acid salt of sitagliptin." *Id.* Petitioner cites the '708 patent's disclosure on reacting one equivalent of sitagliptin with approximately one

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Great Lakes Chem. Corp., 441 F.3d 991, 999 (Fed. Cir. 2006) ("It is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus. . . . There may be many species encompassed within a genus that are not disclosed by a mere disclosure of the genus. On the other hand, a very small genus can be a disclosure of each species within the genus.").

equivalent of phosphoric acid. *Id.* (citing Ex. 1001, 6:29–55). And Petitioner cites Dr. Chorghade's testimony that sitagliptin can only be mono-protonated at sitagliptin's primary amine so that the DHP salt forms "every time." *Id.* (citing Ex. 1002 ¶ 76); *see also* Ex. 1002 ¶ 77 (noting, with no further analysis, that Example 7 of WO '498 is a 1:1 hydrochloride salt). At institution, we observed that Petitioner's position was "light" on analysis for the claimed stoichiometry. Inst. Dec. 53. But we instituted trial, as there was some preliminary support for the position that a 1:1 stoichiometry was inherent, and because, at that time, Patent Owner offered in rebuttal only attorney argument about different protonation states and stoichiometric ratios. *Id.* at 53–54.

In its Response at trial, Patent Owner contends that Petitioner "cannot and does not assert that these references [(WO '498 or the related '871 patent)] expressly disclose" 1:1 sitagliptin DHP. PO Resp. 6–7. And, Patent Owner argues, Petitioner's critical assumptions necessary to prevail on anticipation have now been proved incorrect. *Id.* Thus, whether Petitioner's theory is based on lists or "envisaging" the claimed subject matter, or on "inherency," Patent Owner contends the challenge fails. *Id.* at 7–19.

According to Patent Owner, the unrebutted evidence shows that the salt formation here is unpredictable, it involves "trial and error" processes, and that, absent sufficient detail, a POSA has no way of knowing whether any particular salt within a genus of potential salts will form at all. *Id.* at 8–10 (citing, *e.g.*, Ex. 2103 ¶¶ 163–71, 86–92; Ex. 2127 ¶ 15; Ex. 2042, 5 ("No predictive procedure to determine whether a particular acidic or basic drug would form a salt with a particular counter-ion has been reported in the

literature"); Ex. 2051, 116:22–117:3 (Dr. Chorghade admitting salt formation lacks predictability and is a "trial and error process")). Patent Owner points out that WO '498 does not expressly describe any phosphate salts of any compound, much less any phosphate salt of sitagliptin—only a hydrochloride salt is shown. *Id.* at 7 (citing Ex. 2103 ¶¶ 72–74; Ex. 1004, 46:1–26 (Example 7)). Also, Patent Owner contends, Petitioner has improperly narrowed the combinations in WO '498 when, in fact, there are millions of compounds and hypothetical salts encompassed by WO '498 broad teachings (e.g., compounds based on Formula I), none of which were reviewed by Dr. Chorghade beyond the "33 compounds" in claim 15 and the preferred "8 counterions." *Id.* at 12–13 (citing Ex. 2103 ¶¶ 77–85).

On this record, Patent Owner argues that the "envisaging" doctrine does not help Petitioner. PO Resp. 8. According to Patent Owner, envisaging the claimed subject matter might apply "[i]f the genus resulting from combining the two lists is 'of such a defined and limited class that one of ordinary skill in the art could at once envisage each member of the genus.'" *Id.* (quoting *Wrigley*, 683 F.3d at 1361) (internal quotation marks and citation omitted). But that is not so here, Patent Owner argues, because the genus is not limited as Petitioner says and "[t]he POSA reading WO '498 cannot envisage—because she does not know—the genus of salts that will form." *Id.* at 8–9; Ex. 2051 (Chorghade dep.) 63:22–64:3 ("Q: You wouldn't know without performing research whether a phosphate salt of sitagliptin would form without doing that work. Right? A. That is correct").

Patent Owner emphasizes another allegedly important distinction. To the extent Petitioner's anticipation theory requires combining reagents to

perform an unpredictable *chemical reaction*, Patent Owner contends there is no similarity to other cases like *Wrigley*, where a "simple combination . . . [of] two chewing gum components" was at issue. PO Resp. 11. According to Patent Owner, the district court in *Shire* recognized such a distinction in rejecting the argument that a POSA would at once envisage the claimed compound from combining and chemically reacting two reagents (L-lysine and d-amphetamine) allegedly among lists in a prior art reference. *Id.* (citing *Shire LLC v. Amneal Pharm., LLC*, 2014 WL 2861430 * 15 (D.N.J. June 23, 2014), *aff'd in part, rev'd in part and remanded*, 802 F.3d 1301 (Fed. Cir. 2015)).[16]

Patent Owner further argues that Petitioner is foreclosed from using the "at once envisage" doctrine to fill in limitations missing in WO '498. PO Resp. 18. As noted by Patent Owner, "[t]he 'at once envisage' test 'does not stand for the proposition that a reference missing a limitation can anticipate a claim if a skilled artisan viewing the reference would at once envisage the missing limitation.'" *Id.* (quoting *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 851 F.3d 1270, 1274–75 (Fed. Cir. 2017) (internal quotation marks omitted)). Because "1:1 sitagliptin DHP" is not described and that salt's "1:1 stoichiometry limitation" is "indisputably

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[16] The district court in *Shire*, in granting summary judgment of no anticipation, distinguished *Wrigley*, finding that the claimed compound "does not appear to be something that you get just by mixing a little L-lysine and a little d-amphetamine together" and "[t]here is no dispute that some chemical reactions have to take place." *Shire*, 2014 WL 2861430 at * 15. The Federal Circuit later reversed and remanded on the issue of induced infringement. *Shire*, 802 F.3d at 1310–11.

missing from WO '498," Patent Owner contends "the Board cannot 'fill in missing limitations simply because a skilled artisan would immediately envision them.'" *Id.* at 18–19 (quoting *Nidec*, 851 F.3d at 1274–75); *see also* Sur-reply 1–4 (addressing further the "envisage" theory).

On inherency, Patent Owner argues that undisputed evidence shows sitagliptin and phosphoric acid also react to form non-1:1 phosphate salts. *Id.* at 14–19. So, Patent Owner contends, Petitioner's and Dr. Chorghade's assertions that a 1:1 DHP sitagliptin salt forms "every time" are demonstrably "wrong." *Id.* at 15 (citing Ex. 2013 ¶¶ 99–102, 113–118); Ex. 1002 ¶ 76. In support, Patent Owner identifies non-1:1 phosphate salts of sitagliptin reported in the literature—salts Dr. Chorghade did not consider. PO Resp. 15 (citing Ex. 2220). And Patent Owner's expert "Dr. Matzger has *actually made* other non-1:1 salts." *Id.* (citing Ex. 2103 ¶¶ 123–176). As Dr. Matzger explains, sitagliptin includes multiple sites that can accept protons, and phosphoric acid is "triprotic"—meaning it can donate up to three protons in an acid-base reaction. *Id.* at 16 (citing Ex. 2103 ¶¶ 103–112). Indeed, as Patent Owner contends, Dr. Matzger formed a 3:2 sitagliptin phosphate salt, as well as a 2:1 salt. *Id.* at 17 (citing Ex. 2103 ¶¶ 123–38, 148–176).[17] According to Patent Owner, other

[17] Dr. Matzger testifies, *inter alia*, that "my experiments have definitively shown that non-1:1 salts can indeed form in chemical reactions between sitagliptin and phosphoric acid. . . . [I]t is my opinion that a 1:1 DHP salt of sitagliptin is not the inevitable result of a chemical reaction between those species." Ex. 2103 ¶ 118. As also explained by Dr. Matzger, Exhibit 2220 (WO 2012/166420 ("WO '420")) depicts, among other things, a salt with

chemistry professors, including Drs. Jerry Atwood and Leonard Chyall, respectively from University of Missouri and Purdue University, also formed non-1:1 salts of sitagliptin and phosphoric acid using conventional salt-screening protocols. *Id.* ("Dr. Matzger reproduced one of the non-1:1 sitagliptin phosphate salts of WO '420 [Ex. 2220] (a salt Dr. Chyall had also produced), and determined—via multiple techniques—it was a 3:2 salt.") (citing, *e.g.*, Exs. 2224, 2225, 2227, 2192; Ex. 2103 ¶¶ 123–135, 148–160). Patent Owner contends the existence of these non-1:1 salts "precludes a finding that the 1:1 salt is inherently anticipated." PO Resp. 17–18; *see also* Sur-reply 5–12 (addressing Petitioner's "inherency" theory).

In Reply, Petitioner restates its view that the claimed salt is found in a combination of two lists in WO '498—sitagliptin "among a narrow list of 33 exemplified compounds" and phosphoric acid in a list of eight preferred acids. Reply 2–5. Petitioner contends that there is no dispute that 1:1 salts would be encompassed by the claims of WO '498. *Id.* at 3. And, in furtherance of its envisaging theory, Petitioner contends that Patent Owner's expert, Dr. Matzger, testified that "you can imagine that the [1:1 phosphoric acid salt] would exist." *Id.* (quoting, in part, Ex. 1025, 146:13–147:5) (brackets added by Petitioner)). According to Petitioner, Patent Owner's emphasis on unpredictability is flawed because the issue is anticipation, not obviousness, and also the claimed 1:1 sitagliptin DHP was "made easily" in

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two molecules of sitagliptin to one molecule of the phosphate anion (a 2:1 salt), as well as a 1:2 salt, with one sitagliptin molecule associated with two phosphate anions. Ex. 2103 ¶¶ 121–122 (citing Ex. 2220, 8 (Compound 3), 16 (Compound 7)).

a salt-screen by one of the inventors who had little work experience at that time. *Id.* at 5.

Petitioner's Reply raises two primary points on inherency. First, that, in methanol-based experiments run years ago by Dr. Chyall, the reaction of phosphoric acid and sitagliptin produced 1:1 sitagliptin DHP—results that Merck allegedly does not dispute. Reply 5–7 (citing Ex. 2225[18]). Petitioner contends that because those experiments used "methanol/ambient conditions" they are consistent with the process in WO '498's Example 7. *Id.* at 6–8 (citing Ex. 2225 ¶¶ 22–52, 72; Ex. 1035 ¶¶ 22–26, 63–67). Second, Petitioner argues that Merck's testing evidence misses the mark because it does not resemble WO '498's Example 7. *Id.* at 9 (citing testimony that Dr. Matzger was "not trying to reproduce anything in the '498" (Ex. 1025, 87:21–88:17)). Insofar as Dr. Matzger's testing used an isopropanol/water solvent, not methanol, Petitioner contends that the test results are less relevant (or irrelevant) to whether the claimed 1:1 sitagliptin DHP is inherent based on WO '498. *Id.* at 8–10; *see also id.* at 3 (arguing "Merck turns to non-prior art evidence (WO420) using different conditions than WO498, to contend that other possible stoichiometries may exist").

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[18] Exhibit 2225 is Dr. Leonard J. Chyall's Declaration (dated Aug. 3, 2010) apparently prepared for an opposition proceeding in Israel, concerning a foreign counterpart to the '708 patent. *See* Reply 6; Ex. 2225 ¶ 1. Merck submitted Exhibit 2225, along with other exhibits containing Dr. Chyall's prior testimony, when it filed its Patent Owner Response. *See* PO Resp. 17 (citing Exhibits 2225, 2192, 2224, and 2227). Petitioner and Dr. Chorghade relied, in the Reply, on some of Dr. Chyall's experiments, particularly those in Exhibit 2225 using methanol. Patent Owner moves to exclude in part Exhibit 2225, which we address in Section III.

b) Whether WO '498 Discloses 1:1 Sitagliptin DHP

(i) Petitioner's Lists & "Envisage" Theories

All the challenged claims require a 1:1 sitagliptin DHP salt, as recited in claims 1 or 2. Ex. 1001, 15:64–16:30 (claim 2 is the (R)-enantiomer of 1:1 sitagliptin DHP). We focus on those claims because whether WO '498 discloses, expressly or inherently, that phosphate salt of sitagliptin with its 1:1 stoichiometry is decisive. *Vergegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987) ("A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.").

It is undisputed that a 1:1 sitagliptin DHP salt is not *expressly* disclosed in WO '498. *See* Tr. 15:7–19; Ex. 2103 ¶ 67. No phosphate salts of sitagliptin, or any of the other thirty-two exemplary DP-IV compounds, are shown in WO '498, nor are there details given about making them. Ex. 2103 ¶¶ 74, 81. Petitioner's declarant, Dr. Chorghade conceded these points on cross-examination. Dr. Chorghade agreed, for example, that he was "not aware of any prior process where sitagliptin and phosphoric acid are being reacted to form a phosphate salt" and that "WO'498 does not disclose a process in which sitagliptin and phosphoric acid have been reactive." Ex. 2283, 50:18–51:6; *see also id.* at 15:2–12.

What WO '498 does describe in some detail are *hydrochloride* salts, made by reacting a different acid (hydrochloric acid) with several of the example DP-IV inhibitor compounds. *See, e.g.*, Ex. 1004, 38–47 (Examples 1–7). One of those compounds is sitagliptin. *Id.* at 47; *see also id.* at 56 (bottom-depicted compound).

It is true that, in Example 7, WO '498 describes a process for making a hydrochloride salt of sitagliptin, which appears to form in a 1-to-1 ratio. *Id.* at 47. On this record, however, we credit Dr. Matzger's testimony that a POSA would not simply conclude that whatever applies for hydrochloric acid and sitagliptin also applies to the many different acids that are disclosed—and phosphoric acid, in particular. *See, e.g.*, Ex. 2103 ¶¶ 103–113. First, hydrochloric acid and phosphoric acid are different for at least the reason that hydrochloric acid has only one proton to donate, whereas phosphoric acid has three. *Id.* ¶¶ 33–34 (citing references), 113 n. 39 ("Since HCl is monoprotic, the 1:1 stoichiometry of Example 7 is irrelevant to the question whether a polyprotic acid could form non-1:1 salts with multiple sitagliptin molecules."). Second, persuasive evidence shows that sitagliptin (and structurally-similar analogues) can, indeed, accept multiple protons. Ex. 2103 ¶ 122 (showing a 1:2 sitagliptin phosphate); *id.* ¶¶ 103–105 (discussing Examples 1–5 of WO '498, in which one molecule of the analogue is protonated by two HCl ions), 108 (testifying on other potential ratios with polyprotic acids); Ex. 1004, 38 (Example 1); Ex. 2051 (Chorghade dep.), 152:21–153:10 (agreeing other example compounds are sitagliptin analogues but declining to concede that they have a non-1:1 stoichiometry). This is consistent with Patent Owner's position and Dr. Matzger's testimony that sitagliptin and analogous compounds have, not just one, but multiple sites that are capable of accepting protons when forming salts. Ex. 2103 ¶¶ 103–104 (showing proton-accepting sites at the primary amine and triazole ring).

Petitioner's "list(s)" and "envisage" theories do not make up for the absence of express disclosure of the claimed 1:1 sitagliptin DHP salt on this record. Even accepting that WO '498 includes a "list" of 33 example active compounds and also a "list" of eight preferred acids as possible counterions to form potential salts with such compounds, there is no "list" that identifies *expressly* all the phosphate salts in any, much less all, the potential stoichiometric ratios. Petitioner does not persuasively argue otherwise. And that fact distinguishes this case from others, where the relevant subject matter was listed expressly. *In re Gleave*, 560 F.3d at 1333, 1338 (holding that the reference "expressly lists" every possible one of the relevant sequences).

Petitioner did not attempt to quantify the breadth of compounds and hypothetical salts encompassed by WO '498's disclosures. Nor does Petitioner rebut Patent Owner's evidence that does. *See, e.g.*, Ex. 2103 ¶¶ 73, 97; Ex. 2051 (Chorghade dep.), 57:2–12 (testifying that he did not attempt to quantify the compounds), 69:11–16 (agreeing, however, that sitagliptin is one of "at least 1,000 compounds" in WO '498). Dr. Matzger testifies persuasively that, even if it were appropriate to limit the genus to the 33 example compounds (not the thousands or millions within Formula I), the potential combinations with the 8 preferred acids (rather than the open-ended list of twenty-six acids), and then accounting for varied stoichiometry, "there would theoretically be approximately 957 salts" that might exist. Ex. 2103 ¶ 97 (describing this as a "conservative[] estimate"). Again, this evidence is uncontested. Whether the disclosure cited by Petitioner is characterized as one list or two, we find that there is no express listing of all

these 950-plus hypothetical salts, much less the specific 1:1 sitagliptin DHP as claimed, sufficient to anticipate claims 1 and 2.

With no express disclosure of all limitations of the 1:1 sitagliptin DHP salt in WO '498, Petitioner cannot fill gaps by arguing a POSA would "envisage" what is missing.[19] *See Nidec*, 851 F.3d 1270, 1274–75; *accord Galderma Labs, L.P. v. Teva Pharm. USA, Inc.*, 799 F. App'x 838, 845 (Fed. Cir. 2020) (holding "the district court was not permitted to 'fill in missing limitations simply because a skilled artisan would immediately envision them.'"). On that point, at the oral hearing, Petitioner sought to pivot the inquiry from envisaging to enablement—whether a 1:1 sitagliptin DHP salt is enabled by WO '498. Tr. 13:24–15:3. But, as we pointed out then, Petitioner's argument conflates anticipation and enablement. *Id.* at Tr. 15:7–16:9. "Whether a prior art reference is enabled is a separate question from whether it discloses, expressly or inherently, the claimed limitations at issue." *See Galderma*, 799 F. App'x at 844 (explaining that "Teva makes the impermissible leap from enablement to disclosure" and "[w]hat a POSA 'envisages,' . . . is undoubtedly a question of disclosure, not enablement").[20]

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[19] This gap-filling is precisely what Petitioner attempts to do. *See, e.g.*, Tr. 12:9–11 (Petitioner, after discussing the two alleged lists, arguing "[s]o the only thing we have to show is whether or not a POSA would envision the 1:1 stoichiometry of the 1:1 DHP stoichiometry and whether it would be able to make it.").

[20] Although Petitioner spent little effort developing argument around Merck's listing of the '871 patent in the Orange Book for Januvia in its papers, Petitioner brought up the Orange Book over ten times at oral hearing. *See, e.g.*, Tr. 14:1–14; *see* Pet. 5, 18 n.8, 66 (Orange Book

Separately, even if the law did not foreclose Petitioner's "envisaging" theory, Petitioner's evidence on it is weak. Dr. Chorghade does not opine that a POSA would "at once envisage" the 1:1 sitagliptin DHP salt. *See generally* Ex. 1002. His initial testimony was, instead, that a 1:1 ratio results "every time" sitagliptin and phosphoric acid are reacted (i.e., inherency). Ex. 1002 ¶ 76; Pet. 18 n.8. Now, Dr. Chorghade states simply that he "agree[s] with Dr. Matzger that looking at Example 7, when replacing phosphoric acid for HCL, a POSA 'can imagine that the [1:1 phosphoric acid salt] would exist.'" Ex. 1035 ¶ 9 (quoting Ex. 1025 (Matzger dep.), 147:3–4) (brackets added by Dr. Chorghade); Reply 3 (same). But, a closer look at Dr. Matzger's testimony, in its more complete context, tells a

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(Ex. 1009) mentioned once in an "Overview" section, once in a footnote, and one other time in an effort to preempt a possible nexus showing because the Orange Book lists multiple patents); Reply (no mentions). We warned the parties that oral hearing is not the place for new argument. Paper 80, 3 (citing *Dell Inc. v. Acceleron, LLC*, 884 F.3d 1364, 1369 (Fed. Cir. 2018)). Nevertheless, as best understood, Petitioner sees the listing of the '871 patent in the Orange Book as evidence of or a concession by Merck that the '871 patent (and equally WO '498) claims, describes, and enables the 1:1 sitagliptin DHP salt. There appears to be no dispute by these parties that the salt would be encompassed by broad claims of those references. And while there is some tension between Merck's Orange Book listing and certain arguments made by Merck here (*see* Tr. 48:9–50:9), for reasons explained in this Decision, we find on this record that there is no express or inherent anticipating disclosure of the 1:1 sitagliptin DHP salt in WO '498 (or the '871 patent). Whether Merck's listing of the '871 patent in the Orange Book was appropriate, and whether claims in the reference are so broad that they fail the written description or enablement requirements of § 112, are not issues for us to resolve in this proceeding.

different story—one that does not persuade us a POSA would have at once envisaged the claimed salt:

> [Q] [W]hen you read the phrase or interpret the phrase 'at once envisage,' how did you interpret that in connection with your analysis?
>
> A. That you can clearly see all the possibilities based on the disclosure.
>
> Q. So, in example 7, where it disclosed a 1:1 HCl salt, can you not clearly see the 1:1 phosphoric acid also being there as a result of the HCl salt?
>
> A. So by looking at that, you can imagine that it would exist but that's different than believing it would exist and that it could be produced. So an organic chemist looking at that could exchange the counterion in their mind, but that's different than understanding what could be produced, what would be possible to make.
>
> Q. So you don't dispute that it actually comes to your mind, the 1:1 phosphoric acid salt based on example 7.
>
> A. Looking at the general disclosure, no. It does not come to your mind.

Ex. 1025, 146:13–147:17 (objections and counsel names omitted). The testimony is, thus, more nuanced than Petitioner's and Dr. Chorghade's limited quotation would suggest. Dr. Matzger does not testify that a POSA would immediately envisage all the possibilities. *Id.* Dr. Matzger further clarified that the claimed 1:1 sitagliptin DHP "does not" come to mind based on WO '498. *Id.* And he distinguished a POSA hypothetically imagining something versus understanding from the disclosure that a particular salt would exist or could be made. *Id.* Paired with Dr. Matzger's unequivocal and repeated testimony elsewhere (*see, e.g.*, Ex. 2013 ¶¶ 91–98) that a POSA would not and could not at once envisage all the possible salts, nor

the claimed 1:1 sitagliptin DHP salt, the isolated "imagine" testimony does not carry the weight Petitioner places on it.

Petitioner's envisaging theory fails for yet another reason. Petitioner does not show that a POSA would "at once envisage each member of th[e] limited class" of phosphate salts allegedly disclosed in WO '498. *See Eli Lilly*, 471 F.3d at 1376. Petitioner's expert did not even "at once envisage" each member of the sub-class of different sitagliptin phosphate salts that can be formed (accepting, for sake of argument, the position that combining the identified non-toxic acids with sitagliptin in WO '498 would constitute a disclosure of all pharmaceutically acceptable salts of sitagliptin). Quite the opposite, Dr. Chorghade testified that sitagliptin forms the 1:1 salt with phosphoric acid "every time." Ex. 1002 ¶ 76. The evidence, however, shows that non-1:1 phosphate salts of sitagliptin, such as 1:2, 2:1, and 3:2 salts, do exist and can be made by conventional techniques—with none of those techniques exempted from WO '498's broad disclosure. *See, e.g.*, Ex. 2103 ¶¶ 122–135, 148–160. In short, the envisaging theory is also undermined by Petitioner's own (initial) position, and its own expert's testimony, that the 1:1 salt is the *only* possible sitagliptin phosphate salt.

In reaching our decision, we need not embrace the distinction about chemical reactions that Patent Owner asks us to draw from the district court's decision *Shire*. PO Resp. 10–11. From a lay- or less-technical perspective, combining ingredients in chewing gum (as in *Wrigley*) may be easier to envisage compared to envisaging compounds that may (or may not) form through chemical reactions. Yet the envisaging inquiry and what would be understood and inferred from the prior art do not turn on a lay-

perspective; they are from the POSA's vantage point. *Acoustic Tech., Inc. v. Itron Networked Solutions, Inc.*, 949 F.3d 1366, 1373 (Fed. Cir. 2020) (explaining that "[e]xpert testimony may shed light on what a skilled artisan would reasonably understand or infer from a prior art reference").

Where the level of technical skill is reasonably high, as here, a POSA might well "envisage" a complex product notwithstanding that chemical reactions are required to make it. To the extent Patent Owner suggests "envisaging" is inapplicable if chemical reactions are involved, we decline to adopt such a rule. On the other hand, the art's predictability, at least in some way, colors the lens through which the POSA reads and understands the art.[21] And here, the evidence is undisputed that making salts like those disclosed in the '708 patent and prior art is an unpredictable endeavor. *See, e.g.*, Ex. 2103 ¶¶ 163–71; Ex. 2042, 5 (describing, as of 2002 in the "Handbook of Pharmaceutical Salts," that "[n]o predictive procedure . . . has been reported in the literature"); Ex. 2051, 116:22–117:3. As best we can, in discerning whether WO '498 discloses the claimed 1:1 sitagliptin DHP salt, this Decision considers the art through the ordinarily skilled person's eyes based on the relevant evidence without either improperly inflating or diminishing their abilities.[22]

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[21] *Cf. In re Baxter Travenol Labs.*, 952 F.2d 388, 390 (Fed. Cir. 1991) (holding "extrinsic evidence may be . . . used to explain, but not expand, the meaning of a reference").

[22] That one of the inventors allegedly "made easily" the claimed salt, as asserted by Petitioner (Reply 5), does not mean that the reaction product was known or predictable. Whether a certain salt-screening protocol might be

For the above reasons, we find that there is no express disclosure of the claimed 1:1 sitagliptin DHP salt in WO '498 sufficient to anticipate claims 1 or 2. The other challenged claims (claims 3, 17, 19, and 21–23) depend from claims 1 or 2, so our finding applies to those claims as well.

(ii) Inherency

"An element may be inherently disclosed only if it is necessarily present, not merely probably or possibly present, in the prior art." *Guangdong Alison Hi-Tech Co. v. Int'l. Trade Comm'n.*, 936 F.3d 1353, 1364 (Fed. Cir. 2019). "[A] limitation or the entire invention is inherent and in the public domain if it is the natural result flowing from the explicit disclosure of the prior art.'" *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1379 (Fed. Cir. 2003) (internal quotation and citation omitted).

Petitioner did not, in the Petition, provide any experimental results or data to show that sitagliptin can only be mono-protonated and will form the 1:1 DHP salt every time when reacted with phosphoric acid. *See* Ex. 2051 (Chorghade dep.) 168:11–169:14 (agreeing the declaration (Ex. 1002) provides no literature or data supporting his opinion that sitagliptin can only be mono-protonated). Neither did Petitioner's expert, even throughout trial, conduct testing to confirm that his earlier opinion is correct.

What Petitioner and Dr. Chorghade do rely on now, however, is testing performed by Dr. Chyall many years ago. Reply 1, 5–8. According to Petitioner, Dr. Chyall's testing (described in Ex. 2225) involved "12

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easy to run is different from predictability of the salts that may (or may not) form upon running it; and, as discussed, the preponderance of the evidence is that screening for actual salts is an unpredictable, trial-and-error process.

methanol-based experiments adhering to the WO498's Example 7" and "each experiment resulted in the 1:1 sitagliptin DHP salt." Reply 1 (citing Ex. 2225 ¶¶ 24, 48, 52). Petitioner highlights, in particular, one experiment in which Dr. Chyall reacted sitagliptin and phosphoric acid (in a 1-to-5.01 molar ratio) in methanol at ambient temperature, and made 1:1 sitagliptin DHP. *Id.* (citing Ex. 2225 ¶¶ 24, 27) (quoting portion of a table related to Sample ID "234584" and "Notebook No. 4063-19-01").[23]

Patent Owner, as an initial matter, contends that this is an untimely new anticipation argument from Petitioner, which the Board should not consider. Sur-reply 6 (citing 37 C.F.R. § 42.23(b)). That is, the notion that a POSA would have adhered to WO '498's Example 7 to make a phosphate salt is not in the Petition and, thus, is a new inherency theory. *Id.* In any event, Patent Owner contends the theory is wrong as Dr. Chyall was not trying to reproduce WO '498 or any example from it, nor did he adhere to Example 7 because there are at least eight changes between Dr. Chyall's testing and Example 7—not the least of which is that Example 7 uses hydrochloric acid, not phosphoric acid. *Id.* at 6–8 (listing eight differences) ("WO498 does not disclose any of these modifications to Example 7, so it cannot support inherency as a matter of law").

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[23] Exhibit 2225 includes a table (Table 1) listing twelve salt formation experiments, and indicates three variables were modified between experiments: API (i.e., sitagliptin)/H_3PO_4 molar ratios for the starting materials (e.g., 3:1, 1:5.01, etc.); Reaction solvent (methanol or methanol/water); and Temperature (ambient, 0°C, 65°C). Ex. 2225 ¶ 24.

As discussed below, whether Petitioner's reliance on Dr. Chyall's testing and a modified Example 7 is new or not, on the merits, Petitioner has not proved inherency by a preponderance of the evidence on this record.

Example 7 of WO '498 is *explicitly* a process for preparing a hydrochloride salt. Ex. 1004, 47. One could run that process 10,000 times and it would never produce any phosphate salt of sitagliptin. Ex. 2283 (Chorghade dep.), 52:17–22 (following Example 7 without modification will only produce the hydrochloride salt). Dr. Chyall did not, thus, "adher[e]" to Example 7 because that example must necessarily be changed to produce any phosphate salt. Reply 1. And, there is no process explicitly described in WO '498 for making *phosphate* salts of sitagliptin (or any compound). Ex. 2283, 50:18–51:6; *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 970 (Fed. Cir. 2001) (explaining that inherency must "flow[] from the reference's explicitly explicated limitations"); *Schering*, 339 F.3d at 1379 (same). Nor are we directed to any explicit disclosure in WO '498 that instructs the POSA to apply the process used with hydrochloric acid (e.g., as in Example 7) with the numerous other preferred or non-preferred acids identified. It may be a possible or even likely option that a POSA could change Example 7 to accommodate a use of phosphoric acid, but inherency does not turn on probabilities. "The inherent result must inevitably result from the disclosed steps; '[i]nherency . . . may not be established by probabilities or possibilities.'" *In re Montgomery*, 677 F.3d 1375, 1379–80 (Fed. Cir. 2012) (citations omitted, alterations in original).

Petitioner also admits that Dr. Chyall's testing involved more than merely swapping hydrochloric acid for phosphoric acid in the Example 7

process[24] (even assuming Dr. Chyall was trying to follow Example 7 of WO '498, and there is no evidence that he was). Patent Owner shows that there were at least half-a-dozen other changes from Example 7, including using "dropwise" acid addition, different reactant concentrations, different reaction times, and a "slurry crystallization." Sur-reply 8 (citing e.g., Ex. 2283, 43:12–45:10, 48:15–49:7). That Dr. Chorghade offers possible explanations for the changes or opines that they should make little difference in the end result (Ex. 1035 ¶¶ 26–42) does not alter the fact that what Dr. Chyall did was not the same process described in Example 7 (even beyond the change from one acid to another).

We agree that Dr. Chyall's testing is, in some respects, closer to WO '498's Example 7 than some of the testing conditions presented by Patent Owner. Similar to Example 7, Dr. Chyall used methanol as the solvent and ambient temperature in some of the cited experiments. *Compare* Ex. 1004, 47, *with* Ex. 2225 ¶ 24. In contrast, Dr. Matzger used, for example, an isopropanol solvent system and heat (70°C). Ex. 1025, 80:1–9, 92:2–6. But, when anticipation is the issue, close is not enough. *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983) (explaining that "[a] prior art disclosure that 'almost'" discloses all the elements arranged exactly as in the claim, "may render the claim invalid under § 103, [but] it does not 'anticipate'") (internal citation omitted). Anticipation is still a doctrine based on "strict identity." *Trintec Indus., Inc. v. Top-U.S.A.*

[24] *See* Tr. 19:6–20 (Q: "It wasn't just swapping out HCL for phosphoric acid, there were changes in the protocol [of Dr. Chyall] even from what's explicitly described in Example 7." Petitioner's Counsel: "Of course.").

Corp., 295 F.3d 1292, 1296 (Fed. Cir. 2002). We conclude Petitioner's theory, inasmuch as it relies on a protocol with several admitted changes from what is actually described in an effort to show inherent anticipation, even if such protocol resembles WO '498's Example 7 in some ways, strays into the realm of obviousness.

For the above reasons, we agree with Patent Owner that Dr. Chyall's experiments are no more the actual, asserted "prior art" than Dr. Matzger's. Sur-reply 6. So, while Dr. Chyall's approach in Exhibit 2225 might be one option a POSA might take if screening for potential phosphate salts of sitagliptin, there are other undisputedly reasonable and conventional approaches a POSA could pursue—including the experimental protocols run by Dr. Matzger. *See, e.g.*, Ex. 2103 ¶¶ 123–176. Such protocols include screening salts in an isopropanol/water solvent, and Dr. Matzger's results show production of 2:1 and 3:2 phosphate salts of sitagliptin in that solvent system. *See, e.g.*, *id.* ¶¶ 123–135 and 148–160 (discussing results on 3:2 salt), 136–138 and 161–178 (discussing results on 2:1 salt). Petitioner does not challenge that Dr. Matzger made these non-1:1 salts. Dr. Matzger also explains persuasively that although his experiments show the creation of several non-1:1 salts, "there is no evidence of any 1:1 salt" in the reaction product he created as evidenced by the absence of certain peaks in X-ray powder diffraction measurements he observed. Ex. 2103 ¶ 167.

Petitioner counters that the non-1:1 sitagliptin phosphate salts cited (and made) by Patent Owner are reported in non-prior art evidence. Reply 3 (citing "WO420" (i.e., Ex. 2220)). That argument is, however, misplaced. Non-prior art evidence can be used to show that certain subject matter is or

is not inherent. *Hospira, Inc. v. Fresenius Kabi USA, LLC*, 946 F.3d 1322, 1329–30 (Fed. Cir. 2020) (agreeing a court can use extrinsic, non-prior art evidence in the inherency analysis); *see Monsanto Tech. LLC v. E.I. DuPont de Nemours & Co.*, 878 F.3d 1336, 1345 (Fed. Cir. 2018) (explaining that evidence on inherency "need not antedate the critical date of the patent").

As for Petitioner's contention (Reply 3) that Dr. Matzger used different conditions than WO '498's Example 7, so did Dr. Chyall in the testing that Petitioner relies upon, as explained above. And Petitioner does not seriously contest that Dr. Matzger's salt-screening conditions were anything but conventional. Tr. 74:6–19 (Petitioner's counsel agreeing that an isopropanol/water salt screen like Dr. Matzger used was a conventional process). Indeed, the preponderance of the evidence shows just that. *See, e.g.*, Ex. 2103 ¶¶ 125, 128 (testifying that Drs. Atwood, Chyall, and Matzger all made non-1:1 phosphate salts of sitagliptin "using conventional methods"); Ex. 1025 (Matzger dep.), 219:1–7 (testifying a POSA would run a salt screen, varying solvents, stoichiometry of the reagents, and temperature); Ex. 2283 (Chorghade dep.), 30:12–31:5 (testifying a POSA would have run a salt screen and known that they could have used isopropanol, ethanol, or methanol as solvents). Even for the methanol solvent that Petitioner treats as sacrosanct and not to be changed, Patent Owner cites evidence that non-1:1 sitagliptin salts also form in methanol. Sur-reply 10 (citing Ex. 2220, 32 (Example 2, showing a 2:1 sitagliptin phosphate salt in a methanol system)); Ex. 2283 (Chorghade dep), 87:8–22 (testifying he has "no opinions" on Exhibit 2220 (WO '420)); Ex. 1025,

221:21–228:5 (testifying about Exhibits 2273 and 2274 and non-1:1 sitagliptin sulfates forming in methanol).

In sum, the evidence—confirmed experimentally and reported in the technical literature—undeniably shows that non-1:1 sitagliptin phosphate salts do exist and that the claimed 1:1 sitagliptin DHP does not form "every time" sitagliptin and phosphoric acid are reacted. Petitioner's criticisms that such evidence applies conditions that do not follow Example 7 of WO '498 as closely as the conditions of Petitioner's relied-upon testing are misplaced because that testing too is changed from what WO '498 explicitly describes. We also find that the experimental results cited by Patent Owner are not mere aberrations based on irrelevant conditions. To the contrary, the evidence shows that the conditions under which non-1:1 salts form are conventional salt-screening techniques that a POSA, acting reasonably, could have pursued. We, therefore, find Petitioner's inherent anticipation theory unpersuasive.

Petitioner has not proved that WO '498 expressly or inherently discloses the subject matter of claims 1 and 2. Thus, we find on this record that claims 1 and 2 are not anticipated by WO '498. The other challenged claims (claims 3, 17, 19, and 21–23) depend from claims 1 or 2, so our finding applies to those claims as well.

E. Anticipation by the '871 patent

Petitioner contends that claims 1–3, 17, 19, and 21–23 are anticipated by the '871 patent. Pet. 31–38. According to Petitioner, the '871 patent is prior art under 35 U.S.C. § 102(e)(2). *Id.* at 31–32.

Petitioner states that "[t]he specifications of the '871 patent and WO '498 are identical in all relevant material respects."[25] *Id.* at 33. Indeed, Petitioner's challenge based on the '871 patent parallels the anticipation challenge based on WO '498. *Id.* at 33–38. Petitioner agreed that, like the parties, the Board should treat WO '498 and the '871 patent "for all intents and purposes as having the same disclosures." Tr. 7:8–13; Reply 1 n.2 (noting that Petitioner's "Reply discusses WO498 and the '871 patent together as WO498").

Petitioner's anticipation challenge based on the '871 patent fails for the same reasons as addressed above for WO '498. *See supra* Section II(D). We, thus, similarly find that Petitioner has not proved by a preponderance of the evidence that the '871 patent anticipates claims 1–3, 17, 19, and 21–23.

F. Obviousness

Petitioner asserts that claims 1–3, 17, 19, and 21–23 would have been obvious over WO '498, or WO '498 in combination with Bastin. Pet. 39–46 (Ground 3),[26] 46–59 (Ground 4). Petitioner asserts that claim 4 would have

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[25] WO '498 and the '871 patent each include an identical claim 15 (depicting 33 compounds); the '871 patent also includes one claim that depicts only sitagliptin and further recites "or a pharmaceutically acceptable salt thereof." Ex. 1007, 36:50–40:48 (claim 15), 41:1–14 (claim 17).

[26] The Petition does not identify claims 1 and 2 as being allegedly obvious over WO '498 alone. *See* Pet. 38–39 (starting obviousness analysis with claim 3). That allegation is implicit in Petitioner's allegation that claims depending from claims 1 and 2 would have been obvious. To satisfy limitations of claims 1 and 2 appearing in the dependent claims, however, Petitioner's WO '498 obviousness challenge relies on Petitioner's

been obvious over the combination of WO '498, Bastin, and Brittain (*id.* at 59–62 (Ground 5)), or just WO '498 and Brittain (*id.* at 62–63 (Ground 6)).

1. Antedation and Application of § 103(c)(1) Exception

All of Petitioner's obviousness grounds rely on WO '498. *See generally* Pet. 38–62. Before reaching the merits of Petitioner's challenge, we address a threshold issue. Patent Owner argues that it reduced to practice the subject matter of claims 1, 2, 17, 19, and 21–23 before WO '498 published. PO Resp. 22–28; Sur-reply 21–22. If Patent Owner prevails on that issue, WO '498 is not § 102(a) prior art, and it is merely a § 102(e) reference. Because it is, however, undisputed that the inventions claimed in the '708 patent and the subject matter of WO '498 were commonly owned by Merck, or under obligation of assignment to Merck, at the time of invention, the exception under pre-AIA § 103(c)(1) would apply. 35 U.S.C. § 103(c)(1). Therefore, if we agree with Patent Owner on the antedation issue, WO '498 cannot be used to show that claims 1, 2, 17, 19, and 21–23 would have been obvious. That would then leave only claims 3 and 4 subject to Petitioner's obviousness challenge.

In an *inter partes* review, the burden of persuasion is on petitioner to prove unpatentability by a preponderance of the evidence, and that burden never shifts to patent owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). The petitioner has the initial burden of production to show that an asserted reference qualifies as prior art

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"predicate" anticipation arguments. Pet. 39–40 (incorporating by reference the reasons advanced for Ground 1 (anticipation by WO '498)).

under 35 U.S.C. § 102. *Id.* at 1378–79. Once a petitioner meets the initial burden, a burden of production shifts to the patent owner to argue or produce evidence that the asserted reference does not render the claims unpatentable, or that the reference is not prior art (e.g., because patent owner actually reduced to practice the invention before the applicable date of the asserted art). *Id.* at 1379–80 (citing *Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1327 (Fed. Cir. 2008)).

Patent Owner argues that it actually reduced to practice the subject matter of claims 1, 2, 17, 19, and 21–23 before WO '498's January 16, 2003, publication date. PO Resp. 22–23; *In re Steed*, 802 F.3d 1311, 1318 (Fed. Cir. 2018) (explaining that actual reduction to practice requires an inventor have "constructed an embodiment or performed a process that met all the limitations" of the invention, and "determined that the invention would work for its intended purpose"). According to Patent Owner, the testimony of inventors Vicky Vydra and Dr. Karl Hansen, and from witness Dr. Rebecca Leigh Schultz, which is further corroborated by documentary evidence, shows the creation of a 1:1 sitagliptin DHP salt in December 2001, with experimental confirmation of the salt's form and stoichiometry documented in early 2002. *Id.* at 23–25 (citing, for example, Ex. 2002 ¶¶ 9–20; Ex. 2103 ¶¶ 46–53; Ex. 2127 ¶¶ 11–14, 16–22 (testifying, *inter alia*, on the confirmed stoichiometry using HPLC); Ex. 2140 ¶¶ 30–31; Ex. 2135 (delivery sheet for 1:1 sitagliptin DHP, indicating a testing date of Mar. 25, 2002, and sent date of Apr. 22, 2002)). This evidence, Patent Owner contends, shows successful reduction to practice of the subject matter of claims 1 and 2. *Id.*; *see also id.* at 25–26 (citing additional and persuasive testimony and documentary

evidence (unrebutted by Petitioner) supporting reduction to practice of the subject matter of claims 17, 19, and 21–23).

This proof of reduction to practice, Patent Owner argues, "means that WO '498 qualifies as prior art only under §102(e)." *Id.* at 27. And, citing the exception under pre-AIA § 103(c)(1) and documents showing Patent Owner's common ownership of the claimed subject matter and WO '498, Patent Owner argues WO '498 is eliminated as a § 102(e) reference from the obviousness inquiry for claims 1, 2, 17, 19, and 21–23. *Id.* at 27–28 (citing agreements requiring assignment from the inventors to Merck, such as in Ex. 2005 (Diddle Decl.), 7–8 (Edmondson agreement), 28–29 (Cypes agreement), 44–45 (Vydra agreement)).[27]

Petitioner does not dispute that Merck reduced 1:1 sitagliptin DHP salts to practice before WO '498 published, nor that Merck commonly owned the relevant subject matter. Petitioner, instead, raises a relatively discrete counterargument. Reply 15–18.[28] According to Petitioner, absent Merck proving an earlier reduction to practice of *hydrates* of the 1:1

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[27] Patent Owner argues these employment "agreements required the inventors to assign the claimed inventions to Merck, which they in fact did." PO Resp. 27 (citing supporting evidence including Exs. 2009 and 2010 (certified assignments)).

[28] Before institution, Petitioner argued that the '708 patent "plainly admits" that WO '498 is prior art by listing it in the "Background of the Invention." Pet. 2. We explained previously why we rejected that position and noted, in any event, that it was not controlling on whether the § 103(c)(1) exception applies. Inst. Dec. 41. Petitioner did not contest our explanation or raise that issue again during trial and, thus, Petitioner appears to have abandoned argument based on the alleged "admitted" prior art status of WO '498. To the extent not abandoned, we adopt and incorporate our prior analysis. *Id.*

sitagliptin DHP salt, Merck's antedation argument fails. *Id.* at 17–18. Petitioner alleges the following: (i) the '708 patent's claims do not exclude hydrates, (ii) WO '498 discloses, as a general comment, that "[s]alts in the solid form may exist in more than one crystal structure, and may also be in the form of hydrates," and (iii) although Merck previously made multiple anhydrous forms of 1:1 sitagliptin DHP, it did not make the crystalline monohydrate of 1:1 sitagliptin DHP until March 26, 2003—about two months after WO '498's publication. *Id.* at 16–18 (citing Ex. 1004, 10:32–34; Ex. 2124 ¶¶ 9 (testifying that, as of January 2003, "no hydrates of the 1:1 DHP salt" had been identified), 14 (describing crystalline monohydrate isolation on March 26, 2003)).

In more plain terms, Petitioner argues that WO '498 shows more of the claimed invention than Merck had actually reduced to practice at the relevant time. Reply 15–18. Hence, Petitioner argues, we should reject Merck's antedation argument because Merck has not proved "priority with respect to so much of the claimed invention as the [prior art] happens to show." *Id.* at 15–16 (quoting *In re Clarke*, 356 F.2d 987, 991 (CCPA 1966) (brackets added by Petitioner)).[29]

It is true, on this record, that Merck had made no hydrates of 1:1 sitagliptin DHP as of the January 16, 2003, publication date of WO '498.

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[29] *See also In re Mantell*, 454 F.2d 1398, 1401 (CCPA 1972) (affirming the Board's decision that antedation evidence was insufficient for certain generic claims where "affidavit evidence shows reduction to practice of much less than the reference shows").

Ex. 2124 ¶ 9. We also agree with Petitioner's position that the challenged claims do not exclude hydrates. In fact, claim 1 includes the clause "or a hydrate thereof."[30] Ex. 1001, 16:14–15. But, in resolving the antedation issue here, we are guided by *Clarke*, which explains that "it is not the entire scope of the claims which is determinative . . . . Rather, *it is how much the reference shows of the claimed invention that is crucial* to the requirement." *In re Clarke*, 365 F.2d at 991 (emphasis added). The dispositive question is, thus, whether the evidence shows Merck's reduction to practice of as much of the claimed invention as is shown in WO '498. *Id.*

As discussed above, WO '498 does not expressly show any phosphate salts of any disclosed compound, much less a phosphate salt of any of the thirty-three example compounds, a phosphate salt of sitagliptin, or the particular 1:1 sitagliptin DHP of the challenged claims. *Supra* Section II(D). WO '498 discloses sitagliptin among many compounds, and salts thereof. Ex. 1004, 55–60. WO '498 actually describes a 1:1 hydrochloride salt of sitagliptin—notably, this salt is *not a hydrate*. *Id.* at 47. And, elsewhere, WO '498 lists several potential salt-forming acids, one of which is phosphoric acid among a sub-list of eight preferred acids. *Id.* at 11:8–15. We find that Merck's undisputed, detailed, and repeated actual reduction to practice of the claimed 1:1 (R)-sitagliptin DHP salts shows more, not less,

[30] Claim 2, which is directed to the (R)-configuration of 1:1 sitagliptin DHP does not include the clause "or a hydrate thereof." Ex. 1001, 16:16–30. Claim 4, however, depends from claim 2 and expressly recites "a crystalline monohydrate" of the 1:1 (R)-sitagliptin DHP—claim 2 must, therefore, also encompass hydrates. *Id.* at 16:47–49.

than what is shown in WO '498 for the claimed subject matter. PO Resp. 23–26; Ex. 2103 ¶¶ 46–62; Ex. 2002 ¶¶ 9–20; Ex. 2103 ¶¶ 46–53; Ex. 2127 ¶¶ 11–14, 16–22; Ex. 2140 ¶¶ 30–31.

Even assuming WO '498's disclosure were sufficient to show the claimed 1:1 sitagliptin DHP, there is no *hydrate* of that salt shown anywhere in the reference. Indeed, as Petitioner's declarant concedes, WO '498 provides no polymorphic data for sitagliptin and none of the WO '498 compounds are disclosed as being synthesized as hydrates. Ex. 2051, 197:22–198:9. Unless WO '498 shows a 1:1 sitagliptin DHP *hydrate*, Merck need not have reduced such a hydrate to practice to antedate WO '498's publication date. *In re Clarke*, 365 F.2d at 991.

Petitioner emphasizes the sole mention of "hydrates" in WO '498, which reads, in full, "[s]alts in the solid form may exist in more than one crystal structure, and may also be in the form of hydrates." Ex. 1004, 10:32–34; Reply 16–17. From this, Dr. Chorghade opines that the POSA "would have expected that (R)-sitagliptin phosphate of Claim 2 exists as a crystalline hydrate." Ex. 1002 ¶ 169. That conclusory opinion, however, does not hold up to scrutiny.

First, *none* of the salts described in WO '498—for sitagliptin or otherwise—are hydrates, as Dr. Chorghade admits. Ex. 2051, 197:22–198:9. Second, there are at least thousands, likely millions, of salts embraced by hypothetical combinations of DP-IV compounds and potential counterions in WO '498. Ex. 2103 ¶¶ 73, 77. The solitary "hydrates" sentence is not specific to sitagliptin (or any particular compound), and we credit Dr. Myerson's testimony that a POSA would not have understood the

sentence as applying to sitagliptin phosphate salts in particular. Ex. 2101 ¶¶ 102, 136. Third, the sentence states that crystalline forms (e.g., hydrates) "may" exist. Ex. 1004, 10:32–34. WO '498 does not show that any such hydrates *do* exist for any disclosed or hypothetical salt (much less a 1:1 sitagliptin DHP), nor is there any guidance in WO '498 on making them. Ex. 2101 ¶¶ 93, 124, 150 (expert opinion supporting this interpretation); Sur-reply 17. And fourth, as discussed in more detail below, the substantial weight of evidence shows that whether any particular salt is even capable of forming as a hydrate is highly unpredictable. Indeed, Dr. Chorghade, when asked if he could "predict with reasonable certainty" whether a hydrate might exist, answered that he "couldn't predict with *any degree* of certainty." Ex. 2051, 257:18–258:11 (emphasis added). We, thus, find more credible the testimony of Merck's expert, Dr. Myerson, that "the POSA would not have understood that [one] statement [in WO '498] as disclosing that every compound, or every one of the disclosed or exemplified compounds of WO '498, can exist as a hydrate." Ex. 2101 ¶ 150.

Petitioner suggests, in a footnote, that WO '498 is presumptively enabling for the hydrated forms of the various salts. Reply 18 n.9. Even if that presumption were appropriate here, we would find it overcome based on a complete absence of examples or guidance in WO '498 about making such hydrates, and the substantial unpredictability concerning whether a hydrate of any specific salt will even form, as discussed below.

Patent Owner and Dr. Myerson explain persuasively that a POSA would not have known or predicted whether particular salts, especially the 1:1 sitagliptin DHP, could crystallize at all, form a hydrate, or form a

monohydrate. Ex. 2101 ¶¶ 58–63 ("The unpredictability of crystalline forms applies equally in the context of solvates and hydrates.") (citing supporting evidence), 146–150, 163–164; *see* PO Resp. 46–47, 50–53. The literature of record firmly supports them. For example, in one of Teva's patents, it notes that "[t]he existence and physical properties of polymorphs, hydrates and solvates is unpredictable." Ex. 2048, 3:3–5. In a publication from 2007 (naming Dr. Chorghade as editor), the authors note that "it is still fair to presume that no method exists to predict polymorphs with a considerable degree of certainty," and that discovery and prediction of such forms is filled with "trial and error, and serendipities." Ex. 2045, 215; *see also* 2047, 10 (observing that it is "not yet possible to predict when materials will crystallize" and that polymorphs "are all too frequently discovered by serendipity"); Ex. 2046, 18 ("Predicting the formation of solvates or hydrates . . . is complex and difficult.").[31] And, on cross examination, Dr. Chorghade agreed that the art was unpredictable on precisely this point: "Q. Do you agree that it is unpredictable which set of experimental conditions will yield a particular crystal form? . . . [A] It is not predictable

[31] We agree with Patent Owner that the unpredictability of forming crystalline polymorphs, including hydrates, has been repeatedly recognized in other matters by the Board and the courts. *See, e.g.*, *Lupin Ltd. v. Janssen Sciences Ireland UC*, IPR2015-01030, Paper 17 at 20 (PTAB Oct. 16, 2015) (finding "it would have been known that preparing hydrates generally was unpredictable"); PO Resp. 41–42 (citing cases); *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1089 (Fed. Cir. 2018) ("The experts of both parties agreed that whether a pharmaceutically suitable crystalline salt will form from a particular acid-base combination is unpredictable."). Our Decision here is, however, based on the evidentiary record in this case.

with any degree of certainty." Ex. 2051, 269:11–20; *see also id.* at 245:21–246:8 (admitting "[i]t was presumably true in 2003 and earlier" that it "wasn't possible to predict when materials will crystallize").

Consistent with this evidence, Merck also provides additional testimony and documentation showing that its actual discovery of a hydrate of 1:1 sitagliptin DHP—a crystalline monohydrate—was unforeseen and arose only after substantial work with other salt forms. For example, one of the inventors, Dr. Wenslow, testifies that even after "over a year of development on the 1:1 DHP salt had taken place, including extensive experiments with the 1:1 DHP salt in both water and aqueous solvent mixtures, . . . the DPP-IV project team had not observed a monohydrate until its surprising and unexpected creation very late in the development cycle." Ex. 2116 ¶ 36 (citing Ex. 2119 (project team memorandum), 1–5, 10–11). Another inventor, Stephen Cypes, testifies on the "unexpected" discovery of the hydrated form while trying to find more efficient synthetic routes to directly crystallize a pure *anhydrous* form, and using an isoamyl alcohol/water solvent. Ex. 2124 (Cypes Decl.) ¶¶ 9–15; PO Resp. 5–6; *see also* Ex. 2101 ¶ 94 (opinion of Dr. Myerson that isoamyl alcohol/water is an unusual solvent system, that he is not aware of its use being reported in the art, and that a "POSA would not have arrived at the particular experimental conditions necessary . . . absent undue experimentation").[32]

[32] Petitioner comments that, irrespective to any non-enablement of a *monohydrate*, claim 1 of the '708 patent and WO '498 encompasses hydrates, not just monohydrates. Reply 18 n.9. But the evidence on

Altogether, we find the preponderance of the evidence shows that Merck reduced to practice at least as much (indeed, more) of the claimed subject matter versus what is shown in WO '498. We disagree that, to antedate WO '498's publication, Merck needed to prove a prior reduction to practice of the 1:1 sitagliptin DHP *hydrate*. Accordingly, WO '498 is only a § 102(e) reference. Based on Merck's undisputed ownership (or ownership right by assignment obligation) at all relevant times of the claimed subject matter and WO '498, that reference is excluded from consideration for obviousness purposes under pre-AIA § 103(c)(1) for claims 1, 2, 17, 19, and 21–23. Without WO '498, Petitioner's § 103 challenge to those claims fails. That leaves claims 3 and 4, for which Patent Owner does not assert a prior reduction to practice, subject to the obviousness challenge.

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unpredictability cited above is not limited to monohydrates; it extends to crystalline forms and hydrates generally. Also, as to other hypothetical hydrates of 1:1 sitagliptin DHP, it is not apparent on this record that any exist. Merck cites evidence that, despite years of research, the '708 patent's monohydrate is the only such form known. Ex. 2101 ¶ 205 (citing support); Ex. 2122, 34 (describing "Single crystal form"); Ex. 2124 ¶¶ 9, 15; Sur-reply 25. As to the alleged enablement through use of isopropanol as a solvent (Reply 24–25), although some evidence indicates a 1:1 sitagliptin DHP monohydrate can form in isopropanol/water (Ex. 2101 ¶ 33 (citing Ex. 1001, 12:61–13:21)) there is also experimental evidence to the contrary, which underscores the unpredictable nature of salt formation. *See, e.g.*, Ex. 2103 ¶¶ 123–78 (Matzger testing creating 3:2 and 2:1 sitagliptin phosphate salts in isopropanol/water); Sur-reply 21 ("[I]n isopropanol/water, Dr. Matzger obtained two crystalline salts outside the scope of any claims.").

2. Claim 3

Claim 3 recites "[t]he salt of claim 1 of structural formula III having the (S)-configuration at the chiral center marked with an *" and further depicts the chemical structure of that (S)-form of the 1:1 DHP salt. Ex. 1001, 16:31–45. Patent Owner does not argue that it reduced to practice the subject matter of claim 3 before WO '498 published. WO '498 is, therefore, available as a § 102(a) reference for purposes of analyzing the alleged obviousness of claim 3.

Petitioner argues claim 3 would have been obvious over WO '498 alone (Pet. 38–41), or over a combination of WO '498 and Bastin (Pet. 56). We gave an overview of WO '498 above (*see* Section II(D)(1)). We provide an overview of Bastin below, then turn to the obviousness analysis.

a) Overview of Bastin (Exhibit 1006)

Bastin is a publication from 2000 related to "[s]election of an appropriate salt form for a new chemical entity," giving a chemist "the opportunity to modify the characteristics of the potential drug substance and to permit the development of dosage forms with good bioavailability, stability, manufacturability, and patient compliance." Ex. 1006, 1 (Abstr.). According to Bastin, "[w]here possible, a range of salts should be prepared for each new substance and their properties compared during a suitable preformulation program." *Id.*

Bastin teaches that "the choice of salt is governed largely by the acidity or basicity of the ionisable group," but that "safety" and "drug indications" should also be considered. *Id.* at 2. According to Bastin, "[t]he vast majority of salts are developed to enhance aqueous solubility of drug

substances," and "[f]or weakly basic drugs substances, salts of an inorganic acid (e.g., hydrochloride, sulphate, or phosphate) . . . could be considered." *Id.* (Table 1 (listing "common pharmaceutical salts" including, among others, hydrochloride, hydrobromide, sulfate, nitrate, and phosphate)). Bastin teaches that "[h]ydrochloride salts have often been the first choice for weakly basic drugs . . . [but] the potential disadvantages of hydrochloride salts may include unacceptably high acidity in formulations (e.g., parenteral products), the risk of corrosion, less than optimal solubility . . . and the potential for poor stability." *Id.*

b) Analysis of Alleged Obviousness

The challenge to claim 3 as obvious over WO '498 alone fails because it is based on Petitioner's "predicate" anticipation challenge to claim 1. Pet. 40–41. For the reasons above (*supra* Section II(D)(2)), we reject Petitioner's challenge to claim 1. Petitioner has, thus, failed to succeed on its "predicate" showing. Pet. 40–41.

We turn next to the challenge to claim 3 as obvious over WO '498 and Bastin. Pet. 56; *see also id.* at 46–56 (claim 1 discussion); Reply 21–23.

Petitioner contends that, "[s]ince WO '498 discloses (R)-sitagliptin and its 'pharmaceutically acceptable salts,' the skilled artisan would have been motivated to optimize the salt." Pet. 51. Petitioner contends a POSA would, in making such salts, have used non-toxic acids because sitagliptin is basic. *Id.* at 51–52; Ex. 1002 ¶ 147. According to Petitioner, because WO '498 and Bastin identify phosphoric acid for use as a possible salt-forming acid with basic drugs, and considering Bastin's salt selection and optimization procedures, the POSA would have formed claim 1's 1:1

sitagliptin DHP. Pet. 53–54. Also, Petitioner argues, "Bastin would have given the POSA motivation to make alternatives to the hydrochloride salt due to its potential problems" and "the combined teachings . . . would motivate the POSA to use the following list of three salts as alternatives to the hydrochloride salt exemplified in WO '498: hydrobromide, sulfate, and phosphate." *Id.* at 53; Ex. 1002 ¶¶ 148–152 (testifying about overlapping acids). At a minimum, Petitioner contends "it would be obvious to try" alternatives, and "making the phosphoric acid salt . . . would have been a matter of routine experimentation." Pet. 55–56.

For the (S)-enantiomer limitation, Petitioner contends that WO '498 describes (R)-sitagliptin, but "WO '498 taught that there are only two configurations ((R) and (S)) and how to synthesize each." Pet. 56 (citing Ex. 1004, 10:3–26, 12:11–14); Ex. 1002 ¶¶ 155–156.

On this record, we find Petitioner's challenge to claim 3 unpersuasive. The Petition does not identify where the recited 1:1 ratio is necessarily satisfied upon the combination of WO '498 and Bastin. Petitioner's reliance on Bastin goes, not to any stoichiometry, but to its disclosure of phosphoric acid, some desired attributes of pharmaceutical salts like better stability, and potential disadvantages to using hydrochloric acid. Pet. 53–56; Ex. 1006. Petitioner, however, cites no specific screening or optimization protocol in Bastin that, combined with WO '498, would have led to a 1:1 sitagliptin DHP, or the 1:1 (S)-sitagliptin DHP of claim 3. Again, the Petition relied on the opinion of Dr. Chorghade that the only possible salt arising from the combination of phosphoric acid and (R)-sitagliptin in WO '498 is one with

the recited 1:1 stoichiometry. Pet. 18 n.8; Ex. 1002 ¶ 76. That is incorrect as discussed above. *Supra* Section II(D)(2).

We are also unpersuaded a POSA would have been motivated to make the 1:1 phosphate salt of (S)-sitagliptin, in particular, and that a POSA would have reasonably believed that salt form would have solved any problem with WO '498's hydrochloride salt of (R)-sitagliptin. To the contrary, we agree with Patent Owner that there were numerous reasons why a POSA would not have made all the choices that would been needed to arrive at the claimed subject matter. Ex. 2103 (Matzger Decl.) ¶¶ 31–34 (testifying persuasively on the differences between hydrochloric acid and phosphoric acid and why they are not interchangeable), ¶¶ 214–218 (no shortcomings with the hydrochloride salt of sitagliptin described), ¶¶ 227–229 (testifying, citing supporting literature, that phosphates were known to reduce solubility and stability versus hydrochloride salts); Ex. 2051 (Chorghade dep.) 193:21:–194:2 (admitting nothing in WO '498 suggests any problem with the hydrochloride salt of sitagliptin); Sur-reply 23–24.

Notwithstanding the above, assuming Petitioner's claim 3 challenge is proposing that it would have been obvious to substitute phosphoric acid for hydrochloric acid, and to run the process of Example 7 but with all the changes to it made by Dr. Chyall, and further assuming a POSA would have made such modifications, that would still not produce the claimed subject

matter.[33] That would, at best, make a 1:1 (R)-sitagliptin DHP. *Supra* Section II(D)(2); Reply 1 (citing Ex. 2225 ¶¶ 24, 48, 52).

Claim 3 is, however, to the (S)-enantiomer of 1:1 sitagliptin DHP. *See Sanofi-Synthelabo*, 550 F.3d at 1086 ("The determination of obviousness is made with respect to the subject matter as a whole, not separate pieces of the claim."). Neither WO '498 nor Bastin show any (S)-configuration nor any racemate (mixture of configurations) of any sitagliptin salt. Ex. 2051 (Chorghade dep.) 176:18–177:10 ("Q. The WO '498 does not identify the S-enantiomer – A. No, it doesn't"). And, significantly, Petitioner "does not explain why the POSA would have been motivated to specifically make the (S)-configuration." PO Resp. 38; Ex. 2103 ¶ 255 ("Dr. Chorghade has failed to explain why the POSA would have been motivated to make the (S)-configuration."); *see In re Stepan*, 868 F.3d 1342, 1345–46 n.1 (Fed. Cir. 2017) ("Whether a rejection is based on combining disclosures from multiple references, combining multiple embodiments from a single reference, or selecting from large lists of elements in a single reference, there must be a motivation to make the combination and a reasonable expectation that such a combination would be successful, otherwise a skilled artisan would not arrive at the claimed combination.").

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[33] As discussed above, this strains the arguments made for claim 3 in the Petition, which provided no specific details about how Example 7 should be changed (e.g., details of the screening protocol, such as in Dr. Chyall's testing), nor any experimental proof that a 1:1 stoichiometry arises "every time." Ex. 1002 ¶ 76.

Petitioner advances no expected or even theoretical benefit to making an (S)-enantiomer of 1:1 sitagliptin DHP. Sur-reply 23 ("Mylan fails to identify any reason why the POSA would have formed a salt of (*S*)-sitagliptin."). And we find WO '498's general disclosure on diastereomers, which again appears in reference that putatively encompasses millions of potential compounds and salts, does not show a motivation to make, with a reasonable expectation of success, 1:1 (S)-sitagliptin DHP specifically as claimed—especially where the evidence (discussed herein) also shows that forming such salts is highly unpredictable. *See, e.g.*, Ex. 2042, 5 ("No predictive procedure . . . reported in the literature"); Ex. 2051, 116:22–117:3 (salt formation is an unpredictable "trial and error process").

For the above reasons, we find that Petitioner has not shown by a preponderance of the evidence that claim 3 would have been obvious.

3. Claim 4

Claim 4 recites the "salt of claim 2 characterized in being a crystalline monohydrate." Ex. 1001, 16:47–48. As noted above, Patent Owner does not argue that it reduced to practice the subject matter of claim 4 before WO '498 published. WO '498 is, thus, available as a § 102(a) reference for purposes of analyzing the alleged obviousness of claim 4.

Petitioner asserts that claim 4 would have been obvious over the combination of WO '498, Bastin, and Brittain. Pet. 59–62 (Ground 5). Petitioner also asserts that claim 4 would have been obvious over WO '498 and Brittain. Pet. 62–63 (Ground 6). WO '498 and Bastin are discussed above. We provide an overview of Brittain below, followed by our analysis.

a) Overview of Brittain (Ex. 1005)

Brittain is a chapter from a book titled "Polymorphism in Pharmaceutical Solids," published in 1999. Ex. 1005, 1–4; Pet. 59. Brittain teaches that "it is estimated that approximately one-third of the pharmaceutical actives are capable of forming crystalline hydrates" and, based on data, "[t]his shows the expected trend in which monohydrates are most frequently encountered, and . . . the frequency decreases almost exponentially as the hydration number increases." Ex. 1005, 6.

b) Analysis of Alleged Obviousness

Ground 6, obviousness over WO '498 and Brittain, relies on a "predicate finding" that claim 2 is anticipated by WO '498. Pet. 62. We disagree that claim 2 is anticipated by WO '498 as explained above. *Supra* Section II(D). Ground 6 fails for that reason, but it is also deficient for other reasons discussed below on Ground 5.

For Ground 5, Petitioner first alleges that "Claim 2's (R)-sitagliptin phosphate would have been obvious over WO '498 and Bastin." Pet. 61. Citing WO '498's disclosure that "[s]alts in the solid form may exist in more than one crystal structure, and may also be in the form of hydrates," Petitioner contends the POSA "would have expected that (R)-sitagliptin . . . exists as a crystalline hydrate." *Id.* (citing Ex. 1004, 10:32–34). Then, pointing to Brittain and Dr. Chorghade's opinion, Petitioner contends that crystalline monohydrates are "frequently encountered" with pharmaceutical substances. *Id.* (citing Ex. 1005, 6 (disclosing "approximately one-third of the pharmaceutical actives are capable of forming crystalline hydrates" and an "expected trend in which monohydrates are most frequently

encountered"); Ex. 1002 ¶ 170). Combined with WO '498's alleged teaching "that hydrates exist of the compounds disclosed therein," Petitioner argues the 1:1 (R)-sitagliptin DHP crystalline monohydrate of claim 4 "would have been obvious to a POSA." *Id.* at 61–62.

Patent Owner responds that Petitioner's "cursory treatment [of claim 4] bears almost no resemblance to the required analysis of obviousness." PO Resp. 39. According to Patent Owner, courts (and the Board) consistently uphold as nonobvious claims to specific crystal forms, including monohydrates, even where the salt is disclosed expressly in the art. *Id.*; *see also* at 41–44 (citing cases recognizing unpredictability with crystalline forms). In any event, Patent Owner argues that Petitioner must show a motivation to make the crystalline monohydrate of claim 4 with a reasonable expectation of success, which Petitioner fails to do. *Id.* at 39–59. Indeed, Patent Owner argues, "Mylan fails to articulate *any* reason why the POSA would have been motivated to pursue a crystalline monohydrate form of 1:1 sitagliptin DHP," and the evidence of record gives reasons that would have discouraged the POSA from doing so. *Id.* at 54–59 (citing known problems with hydrates, such as instability and low solubility; Ex. 1005, 4–6). Patent Owner reiterates that none of the salts shown in WO '498 are hydrates, nor is guidance provided on how to make them. *Id.* at 40–41. And, Patent Owner emphasizes, "[c]rystal formation, including the structure, properties, and way to make any hydrate forms was (and is) unpredictable." *Id.* at 41 (citing, e.g., Ex. 2101 ¶¶ 50–64, 88–91; Ex. 2047, 10). Given the state of the art, and the recognized unpredictability of crystalline salt formation, Patent Owner argues the POSA would not have reasonably

expected to obtain the crystalline monohydrate of 1:1 sitagliptin DHP. *Id.* at 44–53 (citing, e.g., testimony from Dr. Chorghade that a POSA "couldn't predict with any degree of certainty" hydrate formation (Ex. 2051, 257:18–258:11), and agreeing it "is rather difficult to predict how many molecules of water or solvent can be incorporated" (Ex. 2051, 238:8–18)).

Beyond the above, Patent Owner also argues that the unexpectedly favorable properties of claim 4's monohydrate are objective evidence of nonobviousness. *Id.* at 60–64. Such properties include thermal stability, and formulation benefits such as reduced sticking and discoloration. *Id.* at 61–64 (citing, for example, Ex. 2101 ¶¶ 189–201 (analyzing thermal stability of the claimed monohydrate versus hydrated sitagliptin HCl and tartrate)).

We find Petitioner has failed to show by a preponderance of the evidence that claim 4 would have been obvious. We explain below.

As noted by Patent Owner, the Petition provides no rationale to explain why the ordinarily skilled person would have been motivated to make the claimed crystalline monohydrate of 1:1 sitagliptin DHP. PO Resp. 54. Even a generic notion that a POSA might have screened for different polymorphs and hydrates (which Petitioner does not articulate here) would be wanting for sufficient reasoning and evidentiary support. *In re Armodafinil Patent Litig. Inc.*, 939 F. Supp. 2d 456, 500 (D. Del. 2013) (holding that "more than a general motivation to find new crystal forms" is required). Petitioner's expert, Dr. Chorghade, offered no motivation (persuasive or otherwise) in his declaration and admitted that he gave no opinion on why a POSA would have preferred a hydrate of sitagliptin. Ex. 2051, 282:18–283:4 ("I don't think I specifically categorized that they

would have preferred the hydrate."); Ex. 1002 ¶¶ 168–170. And, when Petitioner was asked at the oral hearing to identify where, in the Petition, it had given any reason for the skilled artisan to have made the monohydrate of claim 4, Petitioner was unable to do so. Tr. 32:23–34:16.

In Reply, Petitioner attempts to fill this hole by citing vaguely to pages of testimony from Merck's expert, Dr. Myerson. Reply 23 (citing Ex. 1031, 70:1–72:21). But Dr. Myerson's testimony that a POSA may generally prefer "crystalline substances . . . over amorphous forms" does not explain why the specific hydrate of claim 4 would have been pursued or preferred. Ex. 1031, 72:13–21 (testifying that crystalline forms may be preferred for stability, but amorphous forms are sometimes preferred for solubility); Ex. 2051 (Chorghade dep.), 274:14–275:17 (admitting that amorphous forms "can have advantages relative to crystalline materials"). Nor does Petitioner address the numerous downsides of hydrates that are reported in the literature and cited by Patent Owner. PO Resp. 56 ("[T]he POSA would have had a number of reasons for avoiding hydrates.").

Patent Owner cites undisputed evidence that hydrates are known to exhibit lower solubility (and consequent lower bioavailability), as well as physical instability due to dehydration, among other problems. *Id.* at 59; Ex. 2160, 6; Ex. 2162, 8–9; Ex. 2163, 6; Ex. 2101¶¶ 56–57, 128–132. Even Petitioner's relied-upon Brittain reference catalogs many "problems" and "potential issues around hydrates in the development process." Ex. 1005, 5–6 (listing "lower solubility," "variable potencies," and other "negative consequences" like "tablet capping, chemical instability, discoloration, and more"). Petitioner pinpoints Brittain's teaching that "monohydrates are [the]

most frequently encountered" of the crystalline hydrate stoichiometries, but never grapples persuasively with the problems that accompany hydrates and how that would (or would not) have impacted the POSA's motivation to make the crystalline monohydrate of 1:1 sitagliptin DHP. Pet. 63; Reply 23–24. On the other hand, Dr. Myerson, a professor of chemical engineering from MIT with over 40 years' experience, deals with these issues directly. He testifies persuasively that, considering all the evidence, including the vague disclosure about crystalline forms in WO '498 balanced against the widely-reported problems with hydrates, a POSA would have sought to avoid hydrates and would not have been motivated to make a crystalline monohydrate of 1:1 sitagliptin DHP. Ex. 2103 ¶¶ 127–138.

Petitioner's failure to provide a persuasive motivation for making the crystalline monohydrate of claim 4 would, alone, justify rejecting its obviousness challenge. That, however, is not the only problem with Petitioner's challenge. On the full trial record, Petitioner does not persuade us that the ordinarily skilled person would have made the 1:1 sitagliptin DHP crystalline monohydrate with a reasonable expectation of success.

As discussed above, the preponderance of the evidence shows that forming crystalline salts, including hydrates, was and is highly unpredictable. Dr. Myerson testifies persuasively that "it is unpredictable whether any particular compound will be able to be crystallized" and that no means existed to reasonably predict formation of hydrates—much less the specific 1:1 sitagliptin DHP crystalline monohydrate of claim 4. *See, e.g.*, Ex. 2101 ¶¶ 146–149. Petitioner's expert, Dr. Chorghade, concedes that determining whether hydrates will form is difficult and fraught with

unpredictability. *See, e.g.*, Ex. 2051, 200:1–6, 238:8–18, 245:21–246:6 (admitting it "wasn't possible to predict when materials will crystallize"), 257:18–258 (admitting he "couldn't predict with any degree of certainty" hydrate formation). And the bulk of the technical literature on this record confirms the same. *See, e.g.*, Ex. 2047, 10 ("[I]t is not yet possible to predict when materials will crystallize"); Ex. 2050, 31 n.2 ("It is well known among practising chemists that it is often difficult to crystallize a newly synthesized compound."); Ex. 2049, 2 ("[I]t is still not possible to predict with any reasonable level of confidence the crystal structure of an organic material, much less the existence of polymorphism.").[34] Against this evidence, we find unpersuasive Dr. Chorghade's conclusory opinion that the POSA "would have expected that (R)-sitagliptin phosphate . . . exists as crystalline hydrate." Ex. 1002 ¶ 169.

Petitioner's probability-based argument, relying on Brittain, is also over-stated and unpersuasive. PO Resp. 48. We agree with Patent Owner that Brittain undermines Petitioner's argument insofar as the reference discloses that only "one-third of the pharmaceutical actives [APIs] are capable of forming crystalline hydrates," and that only about half of the hydrates in a public database were monohydrates. *Id.* (quoting 1005, 6). In

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[34] *See also* Ex. 2046, 18 ("Predicting the formation of solvates and hydrates . . . is complex and difficult. . . . There may be too many possibilities so that no computer programs are currently available for predicting the crystal structure of hydrates and solvates."); Ex. 2048, 3:3–5 ("The existence and physical properties of polymorphs, hydrates and solvates is unpredictable"); Ex. 2171, 7:32–37 ("There are no rules exist that allow prediction of whether a compound will exist as solvated forms of an organic solvent.").

other words, contrary to what Petitioner's argument suggests about the prevalence of monohydrates, only about *one-sixth* of APIs (active compounds that have been extensively studied) could form a monohydrate according to Brittain. *Id.*; Ex. 2101 ¶ 157. Dr. Chorghade, on cross examination, agreed with this interpretation of Brittain's data. Ex. 2051, 204:18–205:12. Petitioner's probabilistic argument, especially given that the probability is low, is problematic and unpersuasive in showing a POSA's reasonable expectation of success in forming the particular crystalline monohydrate of claim 4. *See Grunenthal GmbH v. Alkem Labs. Limited*, 919 F.3d 1333, 1341–44 (Fed. Cir. 2019) (affirming finding of no reasonable expectation of success in producing the "Form A" polymorph of tapentadol hydrochloride, despite disclosure of the "Form B" polymorph in prior art and evidence that about 30–35% of the compounds are polymorphic); *see also Lupin*, IPR2015-01030, Paper 17, 20–21 (finding similar probability argument did not show a reasonable expectation of success in formulating a hydrate of darunavir); PO Resp. 48–49; Sur-reply 17–18.

In Reply, Petitioner argues that the crystalline monohydrate can be made using an isopropanol/water solvent. Reply 24–25 (citing testimony of Dr. Matzger that use of isopropanol/water as a screening solvent is "old chemistry" (Ex. 2103 ¶ 149; Ex. 1025, 232:14–19)). Putting aside that this is a new theory based on a hypothetical use of an isopropanol solvent system that we could rightly refuse to consider in determining the alleged obviousness of claim 4 (37 C.F.R. § 42.23(b)), it does not justify a finding in Petitioner's favor. Sur-reply 18.

There are numerous solvents and reaction parameters that a POSA could choose in screening for possible crystalline salts (*see, e.g.*, Ex. 2101 ¶¶ 79, 90–91, 163–164, 166), but

> to have a reasonable expectation of success, one must be motivated to do more than merely vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many choices is likely to be successful.

Grunenthal, 919 F.3d at 1342 (internal quotation marks omitted); *accord Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1365 (Fed. Cir. 2007). Petitioner's new focus on isopropanol/water appears to be rooted in hindsight[35] and also fails because the record shows its use, even assuming it was an obvious solvent choice, does not necessarily result in the claimed crystalline monohydrate of the 1:1 sitagliptin DHP. As discussed above, actual testing shows that reacting sitagliptin and phosphoric acid in an isopropanol/water solvent produces non-1:1 salts. *Supra* Section II(D)(2) (discussing Dr. Matzger's experiments); *see also* Ex. 2127 (Hansen Decl.) ¶ 34 (no hydrate despite use of aqueous IPA (isopropanol), citing Ex. 2131, 18)). And, if isopropanol/water was chosen, Petitioner still fails to explain persuasively why the skilled artisan would have *reasonably expected* the resulting salt to be the claimed crystalline monohydrate.

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[35] Petitioner's focus on isopropanol/water likely arose because the '708 patent describes a preparation of the monohydrate in that solvent. Reply 24–25 (citing Ex. 1001, 8:1–13:21, and noting that "inherency" can be based on the patent). A patent's own disclosure can evidence inherency, but Petitioner's use here looks like hindsight to support the alleged obviousness.

For the above reasons, we disagree that a POSA would have reasonably expected to successfully produce the subject matter of claim 4 from the combination of WO '498, Bastin, and Brittain.

Finally, although we need not reach the alleged unexpected properties of the claimed crystalline monohydrate, such unexpected results are further evidence undermining Petitioner's challenge to claim 4. *See Hamilton Beach Brands, Inc. v. f'real Foods, LLC*, 908 F.3d 1328, 1343 (Fed. Cir. 2018) (holding no need to reach objective indicia of nonobviousness where petitioner had not made a showing necessary to prevail on threshold obviousness issues). Petitioner does *not* contest that Patent Owner's relied-upon results were surprising or unexpected, and Dr. Myerson's supporting testimony, which we credit, indicates that they were. Ex. 2101 ¶¶ 186–214. Rather, Petitioner argues, "1:1 sitagliptin DHP is disclosed in WO498 . . . and other sitagliptin phosphoric acid salts are disclosed in WO498," which Petitioner characterizes as "the closest prior art." Reply 25. So characterized, Petitioner argues Merck's results are insufficient because Merck did not compare the results against the "closest" salts, and instead used "more distant salts *e.g.*, HCl, tartrate, etc." *Id.* Petitioner also contends that "Merck only provides data tied to a single crystalline monohydrate form" of 1:1 sitagliptin DHP, and therefore the results are not "commensurate with the scope" of the claims. *Id.* at 25, 27.

We disagree with Petitioner's above-noted criticisms of the unexpected results evidence. *Id.* at 25–27. The only salt of sitagliptin actually identified in WO '498 is the sitagliptin hydrochloride of Example 7. Ex. 1004, 47. No phosphate salt of sitagliptin is specifically identified, and

no hydrates of any salt are described. Ex. 2101 ¶ 136. Merck's evidence, in making comparisons against, for example, *hydrated* forms of sitagliptin hydrochloride provides a more robust and persuasive comparison than it was even required to make. *Id.* ¶¶ 189–201 (analyzing stability results where water in the claimed monohydrate's lattice does not dehydrate until over 100°C versus dehydration at about 20°C for hydrated sitagliptin HCL and tartrate). "Unexpected results are shown in comparison to what was known, not what was unknown." *Millennium Pharma., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1368 (Fed. Cir. 2017) (holding patent owner, in presenting unexpected results, "was not required to create the glycerol ester, when the product had not been created in the prior art").

Moreover, even assuming a 1:1 sitagliptin DHP salt was identified in WO '498, Merck provides evidence, for example, that anhydrous forms of that salt undergo undesirable form conversion while the crystalline monohydrate of claim 4 unexpectedly does not. Ex. 2101 ¶¶ 202–207; *see also id.* ¶ 210 (unpredictable reduction in "sticking" of the monohydrate versus the anhydrous form). Inasmuch as Petitioner's position would require Merck to have further compared the claimed subject matter to itself, that is not required based on the prior art asserted here. *See Millennium*, 862 F.3d at 1368 (citing, with approval, *In re Geiger*, 815 F.2d 686, 690 (Fed. Cir. 1987) (Newman J., concurring) ("The applicant is not required to create prior art, nor prove that his invention would have been obvious if the prior art were different than it actually was.")).

We also conclude that Petitioner's criticism about Merck testing only one form of the crystalline monohydrate of 1:1 sitagliptin DHP is

unavailing. The testing must be "reasonably commensurate" to claim 4's scope, and there is no requirement to test "every embodiment." *In re Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011). The undisputed evidence here is that, despite Merck's years of research and efforts to identify other forms, "the crystalline monohydrate in the '708 patent is the *only* monohydrate of 1:1 sitagliptin known to exist." Sur-reply 26; Ex. 2101 ¶ 205; Ex. 2122, 34; Ex. 2124 ¶¶ 9, 15. On this record, Merck's testing was reasonable and demonstrated unexpected, advantageous properties of the crystalline monohydrate of claim 4.

For the reasons above, Petitioner has not proved by a preponderance of the evidence that claim 4 would have been obvious.

III. MOTION TO EXCLUDE

Patent Owner moves to exclude three exhibits (or portions thereof). *See generally* Paper 81. Petitioner opposes the motion. Paper 83. Patent Owner moves to exclude Exhibit 2225, the declaration of Dr. Leonard J. Chyall dated August 3, 2010, "to the extent Mylan relies on it." Paper 81, 3. Patent Owner moves to exclude Exhibit 1030, Dr. Chyall's lab notebook, in its entirety. *Id.* And lastly, Patent Owner moves to exclude portions of Exhibit 1035, Dr. Chorghade's Reply Declaration, "to the extent it addresses Exhibit 1030 or Exhibit 2225." *Id.* at 3–4. Patent Owner has the burden of proof to show that it is entitled to the requested relief. 37 C.F.R. § 42.20(c). We deny Patent Owner's motion for the reasons explained below.

A. Exhibit 2225 (Chyall Declaration)

Merck argues Exhibit 2225 is inadmissible for two reasons. First, Merck argues the Board should exclude portions of Exhibit 2225 cited by Mylan because they are hearsay. Paper 81, 3–6. Second, Merck argues Exhibit 2225 is inadmissible expert testimony (citing Fed. R. Evid. ("FRE") 702 and *Daubert v. Merrill Dow Pharm., Inc.*, 509 U.S. 579 (1993) ("*Daubert*")). We disagree Exhibit 2225 should be excluded on these bases.

We overrule Merck's hearsay objection because Merck introduced this exhibit and, despite its argument to the contrary, it too relied on Dr. Chyall's testimony (in Exhibit 2225 and several other exhibits) for the truth of the matters asserted.

In its Response, Merck cited generally to "EX2225" (and other Chyall testimony from prior proceedings in Israel, such as in Exhibits 2192,[36] 2224, and 2227) without qualification, limitation, or objection. *See, e.g.*, PO Resp. 17; Paper 83, 1–4. Merck cited this testimony to support its argument that "Dr. Leonard Chyall, of Purdue University, repeatedly reproduced the same material [i.e., non-1:1 salts of sitagliptin and phosphoric acid]." *Id.* Also, Merck's expert, Dr. Matzger, cited repeatedly to Exhibit 2225, including some of the same portions relied on by Petitioner and Dr. Chorghade. For example, Dr. Matzger, pointing to Dr. Chyall's methanol-based experiments,

[36] Exhibit 2192 (Dr. Chyall's Second Declaration, dated March 7, 2012), for example, also appears to include some of the same details of Dr. Chyall's testimony in Exhibit 2225 on the topic of whether it is possible to prepare non-1:1 phosphoric acid salts of sitagliptin; Mylan cites and Dr. Chorghade relies on Exhibit 2192 as well, but Merck does not move for its exclusion.

writes: "Dr. Chyall, Petitioner Teva's expert in the Israeli opposition . . . used an excess of sitagliptin base in multiple of his experiments as well as tested the influence of excess acid." Ex. 2103 ¶ 126 (citing Ex. 2225 ¶¶ 23–25); *see also id.* ¶¶ 130–131 (citing details of Dr. Chyall's solubility study and those results in Exhibit 2225 ¶ 69). This was plainly reliance on Dr. Chyall's testimony for its truth, and Merck's argument that it was cited merely for non-hearsay purposes and because it allegedly motivated Dr. Matzger's own experiments is not persuasive. Paper 85, 2.[37]

Having relied on Dr. Chyall's testimony for factual details about his salt-forming experiments and the actual results of *some* of those experiments, as Merck does, it's hardly surprising Petitioner responded by citing experimental results in Merck's own exhibit that allegedly support Petitioner's argument—experiments showing formation of 1:1 phosphate salts of sitagliptin when reacted in methanol under certain conditions. Merck's argument that it "could not have foreseen" Mylan's use of Exhibit 2225 in this way is, thus, unpersuasive. Paper 85, 3. Once Merck opted to use Dr. Chyall's testimony as a sword, Petitioner was entitled to respond in kind. *Cf. Caterpillar, Inc. v. Wirtgen Am., Inc.*, IPR2018-01091, Paper 49 at 71 (PTAB Nov. 27, 2019) ("We will not endorse Patent Owner's attempt to use the transcript as a sword for its purposes, and our rules as a shield to

[37] For similar reasons, Patent Owner's citation to Fed. R. Evid. 105 is inapposite. Paper 85, 1. We disagree that Patent Owner's reliance on Chyall's testimony is not for its truth. Accordingly, this is not a situation where there is a permissible non-hearsay use by one party and an impermissible hearsay use by another.

prevent Petitioner from using the same transcript to rebut Patent Owner's contentions."); Paper 83, 1.

As for Merck's contention that Dr. Chyall was originally an expert of joinder petitioner Teva, that reliance on Dr. Chyall was withdrawn after joinder was granted, and that Dr. Chyall was not cross-examined in this case, we recognize that Merck sees this as unfair to it. Paper 81, 5–6. On the other hand, Merck opened the door to Petitioner citing Dr. Chyall's experiments where 1:1 salts were made when Merck cited those very experiments (without noting their results) along with other Chyall experiments where he produced non-1:1 phosphate salts. PO Resp. 17. Moreover, early in this case, Merck suggested to the Board that it may pursue Dr. Chyall's deposition. Ex. 1018, 13:15–14:2. The Board signaled it would promptly handle any disputed request for additional discovery, if raised. Paper 44, 9–10. Yet Merck apparently never requested a deposition of Dr. Chyall, nor sought the Board's further help in resolving any discovery dispute. Paper 83, 12–13. In short, Merck cannot escape that its own actions (and inactions) played a significant role in placing Merck in the position it finds itself now with respect to Exhibit 2225.

Merck also requests exclusion of Exhibit 2225 under FRE 702. Paper 81, 7–10. According to Merck, Dr. Chyall's declaration never mentions WO '498, nor did Dr. Chyall seek to reproduce any examples from that reference. Inasmuch as Dr. Chyall's declaration reflects an attempt to make 1:1, or non-1:1, salt forms of sitagliptin, Merck contends his testimony was specific to issues in the proceedings in Israel and "bears no connection to U.S. inherent anticipation law." *Id.* at 8–9. For at least those reasons, Patent

Owner contends the testimony has no scientific connection to the facts of this case and is unhelpful. *Id.* at 7–10.

We agree with Petitioner that Merck's arguments go the weight of this evidence, not admissibility. Paper 83, 13–15. To the extent there are differences between Dr. Chyall's experiments and the examples in the prior art, or other alleged shortcomings with Dr. Chyall's work, that potentially diminish the scientific connection and relevance to the particular issues here, Merck has pointed those things out. *See, e.g.*, Sur-reply 5–7. And we have considered and weighed such matters in reaching our conclusions. Similarly, to the extent Merck's expert relied on Dr. Chyall's work, but also conducted his own experiments in this proceeding to confirm formation of non-1:1 salts, whereas Dr. Chorghade relied on Dr. Chyall's experiments *without* running his own, that too goes to the weight of the respective testimony. Paper 81, 10. We, thus, overrule Patent Owner's FRE 702 and *Daubert* objection to Exhibit 2225.

B. Exhibit 1030 (Chyall Lab Notebook)

Merck moves to exclude Exhibit 1030 for lack of authentication under FRE 901, violation of 37 C.F.R. § 42.65, and as hearsay. Paper 81, 11–12.

We deny Merck's motion to exclude Exhibit 1030. There is a sufficient showing that this exhibit is an authentic copy of Dr. Chyall's lab notebook, as evidenced by the declaration of Noam Blei (Ex. 1036 ¶¶ 1–3), and based on indicia on the document itself (each page titled "Notebook 4063") in combination with Dr. Chyall's declarations (e.g., Exhibits 2221 and 2225, cross-referencing to "Notebook 4063"); FRE 901(b)(3)-(4) (authentication provided by comparison of expert or trier of fact, or by

distinctive characteristics of the evidence taken together with all the circumstances). Merck did not timely object to Exhibit 1030 under Rule 42.65, so the objection was waived.[38] Paper 68, 2; 37 C.F.R. § 42.64(b)(1). Finally, even if we agreed that the notebook is hearsay, we conclude it was permissible, under FRE 703, for Dr. Chorghade to have relied upon the data therein in forming his opinions. That Patent Owner's own expert relies on similar lab notebooks from Dr. Chyall is sufficient to show that the data therein are the type that experts in this field reasonably rely on in forming technical opinions. *See, e.g.*, Ex. 2103 ¶ 131 (citing and relying on Ex. 2226 ("Chyall Lab Notebook 4031")).

C. Exhibit 1035 (Chorghade Reply Declaration)

Merck moves to exclude Exhibit 1035 because "large portions . . . rely on and/or parrot the inadmissible experiments and conclusions of Dr. Chyall in Exhibits 2225 and 1030." Paper 81, 12. We disagree with Merck for reasons already explained above. Under the circumstances here, it was reasonable for Dr. Chorghade to rely on Dr. Chyall's testing and testimony. Merck's contention that the facts and data in Exhibits 2225 and 1030 are not the sort that experts in this field would reasonably rely upon is undermined by its own expert's testimony. *Id.* at 13; *see* Ex. 2103 ¶ 126 (citing and relying on Ex. 2225), ¶ 131 (citing and relying on Ex. 2225 and Ex. 2226 ("Chyall Lab Notebook 4031")). That Dr. Chorghade may lack "personal

[38] Even if the objection had been timely, the declarations of Drs. Chyall and Chorghade include sufficient information to explain the cited testing and comply with Rule 42.65, which does not specify that the affiant must have performed the testing first hand. 37 C.F.R. § 42.65.

knowledge" about that data because he did not generate it himself goes to the weight of his opinions, not admissibility. Paper 81, 13. And, for similar reasons to those above, we disagree that Dr. Chorghade's Reply Declaration, to the extent it relies on Dr. Chyall's allegedly "unhelpful" testing or testimony, should be excluded under FRE 702. Paper 81, 10, 14–15.

For the above reasons, Merck's Motion to Exclude is denied.

IV. CONSTITUTIONALITY

Patent Owner states: "[T]his IPR should be dismissed as unconstitutional because administrative patent judges are principal officers requiring presidential appointment and Senate confirmation." Sur-reply 26–27. We decline to consider Patent Owner's constitutional challenge, as the issue has been addressed by intervening authority in *Arthrex, Inc. v. Smith & Nephew, Inc.*, 941 F.3d 1320, 1335 (Fed. Cir. 2019), *cert. granted sub nom. United States v. Arthrex, Inc.*, 2020 WL 6037206 (Oct. 13, 2020).

V. CONCLUSION

Based on the information in this record, we conclude Petitioner has not shown by a preponderance of the evidence that claims 1–4, 17, 19, and 21–23 of the '708 patent are unpatentable for anticipation or obviousness.

Claims	35 U.S.C. §	Reference(s)/Basis	Claims Shown Unpatentable	Claims Not shown Unpatentable
1–3, 17, 19, 21–23	102(a), (e)(2)	WO '498		1–3, 17, 19, 21–23
1–3, 17, 19, 21–23	102(a), (e)(2)	'871 patent		1–3, 17, 19, 21–23

3, 17, 19, 21–23	103	WO ’498		3, 17, 19, 21–23
1–3, 17, 19, 21–23	103	WO ’498, Bastin		1–3, 17, 19, 21–23
4	103	WO ’498, Bastin, Brittain		4
4	103	WO ’498, Brittain		4
Overall Outcome				1–4, 17, 19, 21–23

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has not shown by a preponderance of the evidence that claims 1–4, 17, 19, and 21–23 are unpatentable;

FURTHER ORDERED that Patent Owner’s Motion to Exclude is *denied*; and

FURTHER ORDERED that, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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