Trials@uspto.gov
571.272.7822

Paper 18
Date: June 22, 2022

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FREEDOM TO OPERATE, INC.,
Petitioner,

v.

COMPASS PATHFINDER LIMITED,
Patent Owner.

PGR2022-00012
Patent 10,947,257 B2

Before SHERIDAN K. SNEDDEN, TINA E. HULSE, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges.*

HULSE, *Administrative Patent Judge*.

DECISION
Denying Institution of Post-Grant Review
35 U.S.C. § 324

I. INTRODUCTION

Freedom to Operate, Inc. ("Petitioner") filed a Petition requesting a post-grant review of claims 1–23 of U.S. Patent No. 10,947,257 B2 (Ex. 1001, "the '257 patent"). Paper 2 ("Pet."). COMPASS Pathfinder Limited ("Patent Owner") filed a Preliminary Response. Paper 7 ("Prelim. Resp."). With our authorization, Petitioner filed a Preliminary Reply to Patent Owner's Preliminary Response (Paper 15), and Patent Owner filed a Preliminary Sur-Reply (Paper 16).

We have authority under 35 U.S.C. § 324(a), which provides that a post-grant review may not be instituted "unless . . . the information presented in the petition . . ., if such information is not rebutted, would demonstrate that it is more likely than not that at least 1 of the claims challenged in the petition is unpatentable." Upon considering the arguments and evidence presented by the parties, we determine Petitioner has not demonstrated that it is more likely than not that any of the claims challenged in the Petition are unpatentable.

A. Real Parties-in-Interest

In the Petition, Petitioner identifies itself as a real party-in-interest and states that, "[s]olely for purposes of this Petition," Ceruvia Lifesciences LLC and B.More Inc. may be considered real parties-in-interest. Pet. 1. Patent Owner identifies itself as a real party-in-interest. Paper 5, 1.

B. Related Proceedings

Petitioner states that it is unaware of any related matters. Pet. 2. Patent Owner identifies PGR2022-00018, in which Petitioner challenges related U.S. Patent No. 10,954,259 B1. Paper 5, 1.

C. The '257 Patent

The '257 patent "relates to the large-scale production of psilocybin for use in medicine." Ex. 1001, 1:16–17. According to the Specification, psilocybin is a plant-based psychedelic that has been used as an aide for psychotherapy, such as for the treatment of mood disorders and alcoholic disorders. *Id.* at 1:37–40. The '257 patent describes efforts for developing a commercially scaled process of making psilocybin. *Id.* at 1:50–3:3.

The '257 patent describes different psilocybin embodiments, including Polymorph A, Polymorph A′, Hydrate A, and Polymorph B. Each embodiment displays different peak positions at varying relative intensities on an X-Ray Powder Diffraction ("XRPD") diffractogram. *Id.* at Table 1 (XRPD for Polymorph A), Table 2 (XRPD for Polymorph A′), Table 3 (XRPD for Hydrate A), Table 4 (XRPD for Polymorph B). For example, a peak at about 17.5°2θ ±0.1°2θ distinguishes Polymorph A from Polymorph A′, in which the peak is absent or substantially absent. *Id.* at 4:43–48; *see also id.* at 6:39–40 (stating a peak at 17.5°2θ ±0.1°2θ is absent or substantially absent in Polymorph A′). Moreover, Polymorph A′ is distinguishable from Polymorph A by the presence of a peak appearing at 10.1°2θ ±0.1°2θ. *Id.* at 7:59–62; *see also id.* at 5:31–33 (stating a peak at 10.1°2θ is absent or substantially absent in Polymorph A).

According to the '257 patent, psilocybin is a "difficult active to formulate" because it has poor flow characteristics and is used in relatively low doses, which makes it difficult to ensure content uniformity and tableting. *Id.* at 19:61–65. Accordingly, the inventors found that in formulating psilocybin tablets, a non-standard filler—specifically a silicified microcrystalline cellulose—was preferred to achieve a satisfactory product. *Id.* at 20:5–15.

D. Illustrative Claim

Petitioner challenges claims 1–23 of the '257 patent, of which claim 1 is the only independent claim. Claim 1 is illustrative and is reproduced below:

> 1. An oral dosage form comprising:
>
> a therapeutically effective amount of crystalline psilocybin in the form Polymorph A characterized by peaks in an XRPD diffractogram at 11.5, 12.0, 14.5, 17.5, and 19.7°2θ±0.1°2θ, wherein the crystalline psilocybin has a chemical purity of greater than 97% by HPLC, and no single impurity of greater than 1%; and
>
> silicified microcrystalline cellulose.

Ex. 1001, 69:23–30.

E. The Asserted Grounds of Unpatentability

Petitioner challenges claims 1–23 of the '257 patent based on the grounds set forth in the table below.

Claims Challenged	35 U.S.C. §	Reference(s)/Basis
1–23	101	Inoperative Invention

Claims Challenged	35 U.S.C. §	Reference(s)/Basis
1–5, 9, 15, 16, 21	103	Folen,[1] Nichols,[2] Carhart-Harris,[3] Griffiths,[4] Guo,[5] Martin's,[6] Handbook of Pharmaceutical Excipients[7]
6, 8	103	Folen, Nichols, Carhart-Harris, Griffiths, Guo, Martin's, Handbook of Pharmaceutical Excipients, JHU Batch[8]
1–23	112(a)	Enablement

Petitioner also relies on the Declarations of Sven Lidin, Ph.D. (Ex. 1006), James A. Kaduk, Ph.D. (Ex. 1008), Raj Suryanarayanan, Ph.D.

[1] V.A. Folen, *X-Ray Powder Diffraction Data for Some Drugs, Excipients, and Adulterants in Illicit Samples*, 20 J. FORENSIC SCI. 348–72 (1975) ("Folen," Ex. 1002).
[2] D.E. Nichols, *Psychedelics*, 68 PHARMACOL. REV. 264–355 (2016) ("Nichols," Ex. 1003).
[3] R. Carhart-Harris et al., *Psilocybin with Psychological Support for Treatment-Resistant Depression: an Open-Label Feasibility Study*, LANCET PSYCHIATRY, *available at* http://dx.doi.org/10.1016/S2215-0366(16)30065-7 (published online May 17, 2016) ("Carhart-Harris," Ex. 1004).
[4] Griffiths R.R. et al., *Psilocybin Produces Substantial and Sustained Decreases in Depression and Anxiety in Patients with Life-Threatening Cancer: A Randomized Double-Blind Trial*, 30 (12) J. OF PSYCHOPHARMACOLOGY 1181 –1197 (2016) ("Griffiths," Ex. 1027).
[5] M. Guo et al., *Potential Application of Silicified Microcrystalline Cellulose in Direct-Fill Formulations for Automatic Capsule-Filling Machines*, 8 PHARM. DEV. AND TECH. 47–59 (2003) ("Guo," Ex. 1005).
[6] Martin's Physical Pharmacy and Pharmaceutical Sciences, 564 (Patrick J. Sinko et al., 6th ed. 2011) ("Martin's," Ex. 1066).
[7] Handbook of Pharmaceutical Excipients, 129–141 (Raymond C. Rowe et al., 6th ed. 2009) ("Handbook of Pharmaceutical Excipients," Ex. 1065).
[8] Psilocybin created by Dr. David Nichols, identified as "Lot 10415-25" ("JHU Batch") and sent to Triclinic Labs for analysis. *See* Ex. 1017.

(Ex. 1010), Charles L. Raison, M.D. (Ex. 1012), and Brett D. Bobzien (Ex. 1020).

II. ANALYSIS

A. Post-Grant Eligibility

As an initial matter, we must determine whether the '257 patent is eligible for post-grant review. Section 6(d) of the Leahy-Smith America Invents Act, Pub. L. No. 112-20, 125 Stat. 284 (2011) ("AIA") sets forth the post-grant review provisions, which apply only to patents subject to the first-inventor-to-file provisions of the AIA. AIA § 6(f)(2)(A) (stating the provisions of Section 6(d) "shall apply only to patents described in section 3(n)(1)"). Post-grant reviews are only available for patents that issue from applications "that contain[] or contained at any time . . . a claim to a claimed invention that has an effective filing date . . . on or after" March 16, 2013. AIA § 3(n)(1). Moreover, "[a] petition for a post-grant review may only be filed not later than the date that is 9 months after the date of the grant of the patent or of the issuance of a reissue patent (as the case may be)." 35 U.S.C. § 321(c).

Petitioner asserts that the '257 patent is eligible for post-grant review because it has an effective filing date of October 9, 2017, and the petition was filed within nine months of the patent's issue date of March 16, 2021, on December 15, 2021. Pet. 3. Patent Owner does not contest the '257 patent's eligibility in the Preliminary Response. *See generally* Prelim. Resp.

Because the '257 patent claims have an effective filing date after March 16, 2013, and because the Petition was filed within nine months of the '257 patent's issue date on December 15, 2021, we find that the '257

patent is eligible for post-grant review. *See* Pet. 3, 57; *see also* Ex. 1001, codes (45), (63).

B. Person of Ordinary Skill in the Art

Petitioner asserts that a person of ordinary skill in the art "would have had an advanced degree (i.e., a Master's degree with two or more years of experience, or a Ph.D.) in inorganic or organic chemistry, chemical engineering, pharmacology, or a related discipline" and "would be familiar with medicinal chemistry or pharmaceutical chemistry, and with analytical methods to characterize and differentiate solid forms of compounds, particularly XRPD, but also including differential scanning calorimetry ('DSC') and thermogravimetric analysis ('TGA')." Pet. 28 (citing Ex. 1006 ¶ 35). Petitioner further contends that "[a]lternatively, one of ordinary skill could have less education and approximately five or more years of relevant experience." *Id.* Patent Owner does not dispute Petitioner's definition of the level of ordinary skill in the art. *See generally* Prelim. Resp.

Absent opposition from Patent Owner, we adopt Petitioner's definition because it is consistent with the level of ordinary skill in the art reflected by the prior art in this proceeding. *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

The Board applies 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. § 42.200(b) (2019). Under that standard, claim terms "are

generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

Petitioner proposes constructions for two claim terms: "crystalline psilocybin in the form Polymorph A" and "characterized by peaks in an XRPD diffractogram at 11.5, 12.0, 14.5, 17.5, and 19.7°2θ±0.1°2θ." We address each claim term below.

1. "crystalline psilocybin in the form Polymorph A"

Petitioner contends that "crystalline psilocybin in the form Polymorph A" should be construed as "a crystalline form of a *single* polymorphic phase of psilocybin defined by the patentee as Polymorph A." Pet. 7 (emphasis added). Petitioner asserts that "[u]nder this construction, the claimed X-ray powder diffraction ('XRPD') peaks must be the result of reflections from the claimed single polymorph of psilocybin, and not the result of reflections from a mixture of different polymorphs of psilocybin." *Id.* Petitioner argues that the claims support this because "claim 1 uses the singular noun 'form' and the definite article 'the' before 'form' in the claim term 'crystalline psilocybin in the form Polymorph A.'" *Id.* (citing Ex. 1001, 69:27 (emphasis omitted)). Petitioner further contends that the '257 patent's Specification distinguishes Polymorph A from Polymorph A' and this precludes a construction that "permits a mixture of polymorphs that includes Polymorph A-prime." *Id.* at 8–9. Petitioner also argues that its proposed construction accords with the ordinary and customary definition of "polymorph," which is generally agreed to be "a solid crystalline phase of a given compound resulting from the possibility of at least two different arrangements of the molecules of that compound in the solid state." Pet. 9 (citing Ex. 1006 ¶ 18; Ex. 1031, 428).

Patent Owner opposes Petitioner's proposed construction, asserting that it is inconsistent with the intrinsic record of the '257 Patent. Prelim. Resp. 4 (citing *Immunex Corp. v. Sanofi-Aventis U.S. LLC*, 977 F.3d 1212, 1221 (Fed. Cir. 2020)). Patent Owner contends that "[t]he inventors defined the phrase 'crystalline psilocybin in the form Polymorph A' (or 'Polymorph A') in the '257 Patent to mean 'a crystal form of psilocybin having the X-ray powder diffraction (XRPD) peaks listed in claim 1.'" *Id.* Patent Owner notes that "Polymorph A" has no plain and ordinary meaning in the art and asserts that the claim language supports its construction. *Id.* at 4–5 (citing Ex. 1001, claim 1). Patent Owner further argues that the '257 patent's Specification and the prosecution history support its construction. *Id.* at 5–8 (citing Ex. 1001, 4:5–5:36, 6:34–8:10, 11:40–12:37, 10:5–11:5; Ex. 2024, 2; Ex. 1060, 7; Ex. 1062, 2, 6). Patent Owner also argues that its construction is consistent with prior claim construction decisions. *Id.* at 8–9 (citing *In re Armodafinil Patent Litigation*, MDL No. 10-md-2200-GMS, 2011 WL 9158436, at *1 (D. Del. July 25, 2011); *Willowood USA, LLC. v. BASF SE*, No. IPR2018-01096, Paper 10 (P.T.A.B. Nov. 29, 2018) (Ex. 2002)). Patent Owner contends that Petitioner's proposed construction is unsupported by the intrinsic evidence and seeks to supplant the inventors' express definition. *Id.* at 9–11.

We agree with Patent Owner's proposed construction, as it is most consistent with the intrinsic evidence. The claim language makes clear that "Polymorph A" is "characterized by" the specific peaks set forth in claim 1. Ex. 1001, claim 1. Thus, regardless of the alleged conventional definition of a "polymorph," urged by Petitioner, the inventors are entitled to act as their own lexicographers to define "Polymorph A" according to the recited peaks on the XRPD diffractogram. *See Honeywell Int'l, Inc. v. Universal Avionics*

Sys. Corp., 493 F.3d 1358, 1361 (Fed. Cir. 2007) ("When a patentee defines a claim term, the patentee's definition governs, even if it is contrary to the conventional meaning of the term."). That the Specification consistently refers to "Polymorph A" as a proper noun and describes Polymorph A as "characterized by" the recited peaks in an XRPD diffractogram further highlights the inventors' clear intent to act as their own lexicographer. *See, e.g.*, Ex. 1001, 4:4–5:36; *Merck & Co. v. Teva Pharms. USA*, 395 F.3d 1364, 1370 (Fed. Cir. 2005) ("When a patentee acts as his own lexicographer in redefining the meaning of particular claim terms away from their ordinary meaning, he must clearly express that intent in the written description.").

Finally, during prosecution of the '257 patent application, the examiner rejected original claim 1 as indefinite because it did not define "Polymorph A," and required one to "refer to the specification to determine what is Polymorph A." Ex. 1060, 7. Patent Owner then amended the claims to define Polymorph A by adding the specific XRPD peaks recited in claim 1. Ex. 1062, 2; *see also id.* at 6. Thus, we find the intrinsic evidence supports Patent Owner's proposed construction.

We are not persuaded by Petitioner's arguments to the contrary. That claim 1 uses the singular noun "the form Polymorph A" is not inconsistent with Polymorph A being defined by the recited diffractogram peaks. *See* Pet. 7. Nor is the Specification's use of "Polymorph A" and "Polymorph A'" inconsistent with Patent Owner's construction. *See id.* at 8–9. Even if Polymorph A is a mixture of Polymorph A' and Polymorph B, as Petitioner suggests (*see id.* at 35), Petitioner has not explained why that precludes referring to the two forms of psilocybin separately as "Polymorph A" and "Polymorph A'," particularly when Polymorph A is characterized by

different XRPD peaks than Polymorph A'. *See* Ex. 1001, Table 1 (XRPD peaks of Polymorph A), Table 2 (XRPD peaks of Polymorph A').

Accordingly, having considered the parties' respective arguments and evidence, we construe "crystalline psilocybin in the form Polymorph A" to mean "a crystal form of psilocybin having the X-ray powder diffraction (XRPD) peaks listed in claim 1" and we decline to limit the term to a single polymorphic phase of psilocybin.

2. "characterized by peaks in an XRPD diffractogram at 11.5, 12.0, 14.5, 17.5, and 19.7°2θ±0.1°2θ"

Petitioner argues that the limitation "'characterized by peaks in an XRPD diffractogram at 11.5, 12.0, 14.5, 17.5, and 19.7°2θ±0.1°2θ' should be construed to mean '[i]dentifiable by reference to an X-ray diffractogram that discloses within normal experimental error peaks at 11.5, 12.0, 14.5, 17.5 and 19.7±0.1°2θ.'" Pet. 9–10. According to Petitioner, "[t]he phrase 'characterized by peaks in an XRPD diffractogram' could be construed to require either a precise match between XRPD diffractogram peaks, or to require that the XRPD diffractogram peaks be identifiable by reference to an X-ray diffractogram that discloses the referenced peaks within normal experimental error." *Id.* at 10. Petitioner contends that the latter "allows for experimental error and variation that would be expected by a person of ordinary skill, [and] is the one that fits best with the specification and the way a person of ordinary skill would read an XRPD diffractogram." *Id.*

Petitioner asserts that this limitation is not defined in the Specification and the Specification does not explain a basis for the claimed range of the peak locations ("±0.1°2θ"). *Id.* Petitioner argues that Dr. Lidin explains how "slight experimental errors and variation in XRPD patterns and exact peak locations and intensities can be expected, depending on, for example,

measurement techniques or the presence of other crystalline materials." *Id.* (citing Ex. 1006 ¶¶ 42, 50, 62–66, 73). Moreover, Petitioner asserts that "[s]uch factors can insignificantly shift single peaks in XRPD patterns for a single polymorph, but a person of ordinary skill would look at the XRPD pattern as a whole to determine if any one shift is likely a result of experimental variation." *Id.* at 10–11 (citing Ex. 1006 ¶¶ 42, 50, 62–66, 73). Petitioner further cites two district court cases involving related patents to support its argument that experimental error should be factored into the claims. *Id.* at 11–12 (citing *Astrazeneca AB v. Reddy's Laboratories, Inc.*, No. 11-2317, 2013 U.S. Dist. LEXIS 62149 (D.N.J. May 1, 2013) (Ex. 1032; *Astrazeneca AB v. Andrx Labs, LLC*, No. 14-8030, 2017 U.S. Dist. LEXIS 3990 (D.N.J. Jan. 11, 2017).

In response, Patent Owner contends that the limitation should have its plain and ordinary meaning without further construction and that "Petitioner provides no justification for departing from the recited claim language." Prelim. Resp. 11–12. Patent Owner argues that "[t]he XRPD peaks are expressly recited with a standard precision accepted within the art of '± 0.1 °2θ' and do not require further construction." *Id.* at 12. Patent Owner notes that the Specification only discloses a variance of ±0.10°2θ, and if it wanted a broader range, it could have used the term "about" to modify the XRPD peak values recited in the claims. *Id.*

Patent Owner further contends that, according to the United States Pharmacopeia ("USP") the "recited variance of '±0.1°2θ' is recognized in the art as the established experimental error for XRPD peaks." *Id.* at 13–14 (citing Ex. 2005, 2007). Moreover, Patent Owner asserts that "courts have regularly relied on the USP when construing claims directed to the XRPD peaks to have a variance of '± 0.1 °2θ' while rejecting proposed claim

constructions that seek to impermissibly expand claim scope under the guise of 'normal experimental error.'" *Id.* at 14–15 (citing *GlaxoSmithKline Intellectual Prop. Mgmt. Ltd. v. Sandoz, Inc.*, No. 11-1284-RGA, 2013 WL 1163759 (D. Del. Mar. 20, 2013) (Ex. 2006)).

Having considered the parties' respective arguments and evidence, we find Patent Owner has the better position. Although we agree with Petitioner that some degree of experimental error should be factored into the specific peaks of a diffractogram, the claim language already does so by expressly reciting a variance of "±0.1°2θ." *See* Ex. 1001, claim 1. Construing the claims to include an additional degree of variance would effectively read out the "±0.1°2θ" limitation of the claims. *See Merck & Co. v. Teva Pharms. USA, Inc.,* 395 F.3d 1364, 1372 (Fed. Cir. 2005) ("A claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so."). Moreover, we note that the express recitation of a specific variance distinguishes the '257 patent claims from the claims of the *Astrazeneca* cases cited by Petitioner, which did not recite such a variance. *See* Pet. 11–12.

In addition, the Specification consistently refers to a variance of ±0.1°2θ whenever it refers to peaks on a diffractogram. *See generally* Ex. 1001, 3:58–5:24. Petitioner acknowledges that the claims recite a range of peak locations, but argues that the Specification "does not explain the basis for the claimed range." Pet. 10. Petitioner, however, does not explain why the Specification would need to explain that basis, particularly if a person of ordinary skill in the art would understand that ±0.1°2θ is an acceptable variance for XRPD.

To support their respective constructions, both parties cite UPS Chapter <941> on XRPD, albeit from different years. *Compare* Ex. 1023,

427 (USP 35, official as of May 1, 2012)*, with* Ex. 2005, 3 (USP 24, official as of Jan. 1, 2000). Patent Owner cites USP 24, which states "2θ values 'should typically be reproducible to ± 0.10' or a total variance of 0.20 degrees." Prelim. Resp. 13–14 (quoting Ex. 2005, 5[9]). Petitioner's expert, Dr. Lidin, on the other hand, cites USP 35 and contends that "USP 35 <941> accepts a tolerance of ±0.20°2θ in XRPD data generated using modern techniques and instrumentation." Ex. 1006 ¶ 65 (citing Ex. 1023). Thus, from the parties' arguments alone, the USP would appear to be inconsistent.

Upon further inspection, however, we find the USP supports Patent Owner's construction. Unlike Patent Owner, Dr. Lidin does not provide a pincite or quote to Exhibit 1023 that points us to where the USP states it accepts a tolerance of "± 0.20°2θ," as Dr. Lidin asserts. *See* Ex. 1006 ¶ 65 (citing Ex. 1023). Nevertheless, in our own review of Exhibit 1023, we find USP 35 actually states that "[t]he agreement in the 2θ-diffraction angles between specimen and reference is within 0.2° for the same crystal form." Ex. 1023, 430. Thus, contrary to Dr. Lidin's testimony, the USP *does not* state that it accepts a tolerance of "± 0.20°2θ" (i.e., for a total variance of 0.4°2θ). *See* Ex. 1006 ¶ 65. Rather, by stating the agreement is "within 0.2" degrees, USP 35 is consistent with USP 24, cited by Patent Owner, which states that "[a]greement between sample and reference should be within the calibrated precision of the diffractometer for diffraction angle (2θ values should typically be reproducible to ± 0.10°2θ *or 0.20 degrees*)." *See* Ex. 2005, 5 (emphasis added). In other words, according to the USP, the calibrated precision of the diffractometer should be within ±0.1°2θ

[9] We cite the exhibit page number in the bottom right corner of the exhibit.

experimental error, not "± 0.20°2θ," as asserted by Petitioner's expert, Dr. Lidin. We note that the court in *GlaxoSmithKline* came to the same conclusion when interpreting this statement from the USP:

> The U.S. Pharmacopeia is an authoritative scientific treatise, and it makes most sense for the tome to provide only a single margin of error with regard to a measuring technique used in a field dependent on precision. Understanding '±0.10°2θ or 0.20 degrees' to provide a singular margin of error results in an internally consistent, if redundant, interpretation."

See Ex. 2006, 3

Thus, having considered the arguments and evidence presented, we find the intrinsic and extrinsic evidence support construing the recited variance of "±0.10°2θ" according to its plain and ordinary meaning without additional experimental error.

3. Remaining Claim Terms

We determine that it is unnecessary to expressly construe any other claim terms for purposes of rendering this Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

We now turn to the substantive patentability challenges set forth in the Petition.

D. Inoperative Invention and Enablement

Petitioner asserts that claims 1–23 of the '257 patent are unpatentable under 35 U.S.C. §§ 101 and 112[10] for claiming an inoperative invention.

[10] Petitioner makes additional arguments that claims 1–23 are not enabled. *See* Pet. 52–55. We address those arguments separately below.

Pet. 34–38. Patent Owner opposes Petitioner's assertions. Prelim. Resp. 16–19.

Petitioner argues that, under its proposed construction, "claim 1 requires a 'crystalline form of a single polymorphic phase of psilocybin defined by the patentee as Polymorph A,' which is 'identifiable by reference to an X-ray diffractogram that discloses within normal experimental error peaks at 11.5, 12.0, 14.5, 17.5 and 19.7±0.1°2θ.'" *Id.* at 35. Petitioner contends that no such polymorph of psilocybin exists because "Polymorph A" is a mixture of Polymorph A' and Polymorph B. *Id.* at 35–38 (citing Ex. 1006 ¶¶ 4, 29, 31, 47–54; Ex. 1008 ¶¶ 4, 19–23, 46, 47, 50). In view of this discovery, Petitioner argues that claim 1 is not "useful" because it is incapable of being practiced and is therefore invalid as inoperative. *Id.* at 38. Petitioner also contends that for the same reasons, the '257 Patent is invalid as not enabled under § 112 because it is "impossible to practice." *Id.*

Because Petitioner's argument hinges on its incorrect construction of "Polymorph A," which we rejected above, we are not persuaded that such a construction should be applied to render the claims unpatentable for the same reasons explained above. *See supra* Section II.C.1. Accordingly, we determine Petitioner has not shown it is more likely than not that any of the challenged claims are unpatentable under § 101 as inoperable or under § 112 as not enabled.

E. Obviousness

Petitioner asserts claims 1–9, 15, 16, and 21 of the '257 patent are unpatentable as obvious over "Folen (Ex. 1002) in view of Nichols (Ex. 1003), or alternatively Carhart-Harris (Ex. 1004), and Griffiths (Ex. 1027), together with the Handbook of Pharmaceutical Excipients (Ex. 1065), Siven (Ex. 1079); and, alternatively or in conjunction with, Guo

(Ex. 1005)." Pet. 39–40.[11] Patent Owner opposes Petitioner's challenge. Prelim. Resp. 19–27.

Having considered the evidence and argument presented by the parties, we determine Petitioner has not shown it is more likely than not that any of the challenged claims are unpatentable as obvious over the cited art.

Although Petitioner relies on a number of different prior art references for its obviousness challenge, we need only address the disclosure of Folen for purposes of this Decision.

1. Folen (Ex. 1002)

Folen is an article entitled, "X-Ray Powder Diffraction Data for Some Drugs, Excipients, and Adulterants in Illicit Samples," published in the *Journal of Forensic Science*. Ex. 1002, 1. According to Folen, "[t]he development of new compounds with the potential for drug abuse necessitates a continuous accumulation of analytical data in the forensic laboratory." *Id.* Moreover, identifying excipients and adulterants in drug samples provides a database that can be used for intelligence purposes. *Id.* Accordingly, Folen states that "[t]he purpose of the present paper is to present X-ray powder diffraction data not available in the literature." *Id.*

Table 2 of Folen provides complete X-ray diffraction data and relative intensities of the peaks for 73 different compounds, including psilocybin (*id.* at 366). *Id.* at 353–69. Folen provides d-spacing values for psilocybin, which can be converted to °2θ (as recited by the '257 patent claims) using

[11] We note that this statement of the obviousness challenge appears inconsistent with the summary of the obviousness grounds on pages 4–5 and the claim chart on pages 43–52 of the Petition. We need not resolve these inconsistencies, however, for purposes of this Decision.

Bragg's Equation. Pet. 15. Petitioner provides the equivalent °2θ values for the pertinent peaks of psilocybin in the chart below:

Folen d-spacing value	**2θ**
7.74	11.4
7.40	12.0
6.13	14.4
5.00	17.7
4.56	19.5

Id.

2. Analysis

A patent claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed subject matter 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 to which the subject matter pertains. *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 skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

Petitioner relies solely on Folen—along with the testimony of its experts regarding Folen—as allegedly teaching the recited XRPD peaks of Polymorph A in claim 1. Pet. 40–41, 43 (citing Ex. 1006 ¶¶ 38–42, 61–66, 71–75; Ex. 1008 ¶ 48). Referring to the converted peaks taught by Folen, Petitioner asserts that "[t]he first three of these peaks [i.e., 11.4, 12.0, and 14.4] are directly within the claimed range of ± 0.1°2θ. The second two peaks [i.e., 17.7 and 19.5] are within ± 0.2°2θ." Pet. 40. Thus, Petitioner

acknowledges that Folen's peaks at 17.7 and 19.5 are not within the recited range of "17.5, and 19.7°2θ ± 0.1°2θ" as required by claim 1. Ex. 1001, 69:26–27.

Nevertheless, Petitioner argues that "[a] person of ordinary skill would also recognize in reading Folen that it used older equipment and manual methods of assigning d-values, which might create some variability in measuring exact peak locations." *Id.* Petitioner then continues, stating "[f]or this and the other reasons explained in the Lid[i]n Declaration, these latter two peaks would be seen by a person of ordinary skill in this field as disclosing the claimed peaks at 17.5 and 19.7°2θ ± 0.1°2θ." *Id.* (citing Ex. 1006 ¶¶ 38–42, 61–66, 71–75). Petitioner also contends that Dr. Kaduk "confirms that the psilocybin analyzed by Folen was characterized by XRPD reflections that were consistent primarily with Polymorph A-prime, although both Polymorph B and Hydrate A also were detectible. . . . [and] undoubtedly were present in the Folen sample." *Id.* (citing Ex. 1008 ¶ 48). According to Petitioner, Dr. Kaduk's analysis of Folen "demonstrates that these three predominant crystalline forms of psilocybin existed as early as 1975, and that variable amounts of these three phases could be expected in historical samples of psilocybin made and used in clinical trials before 2017." *Id.* (citing Ex. 1008 ¶ 48).

We are not persuaded that Petitioner has shown sufficiently that Folen teaches or suggests the recited peaks at 17.5 and 19.7°2θ ± 0.1°2θ. First, as Petitioner admits, Folen's teaching of peaks at 17.7 and 19.5°2θ are not within ±0.1°2θ of 17.5 and 19.7°2θ. Pet. 40. Petitioner attempts to convince us, however, that a person of ordinary skill in the art would recognize that Folen's peaks at 17.7 and 19.5 teach the required peaks at 17.5 and 19.7± 0.1°2θ. Petitioner's argument fails for several reasons.

First, Petitioner argues that a person of ordinary skill in the art would understand that Folen used older equipment that "*might* create some variability in measuring exact peak locations." Pet. 40 (emphasis added). Notwithstanding the uncertainty that there "might" be some variability, Petitioner cites no support for this statement. But even if Petitioner had cited its expert's testimony, Dr. Lidin's testimony suffers from the same fatal flaw. Dr. Lidin claims that "[o]ther researchers have noted potential error in analog data recordings can be caused by uneven movement of the chart, limited precision in reading the chart, and time-constant and scanning-speed distortion." Ex. 1006 ¶ 42. Dr. Lidin also claims that "in older machines, initial synchronization between the diffractometer and chart recorder as well as pen-response time can create precision errors." *Id.* Dr. Lidin, however, cites no objective evidence to support his assertions. As Petitioner knows, we give little to no weight to such unsupported expert testimony and therefore do not find this argument persuasive. *See* 37 C.F.R. § 42.65(a) (stating opinion testimony that does not disclose underlying facts or data "is entitled to little or no weight"); *see also Rohm & Haas Co. v. Brotech Corp.*, 127 F.3d 1089, 1092 (Fed. Cir. 1997) (nothing in the Federal Rules of Evidence or Federal Circuit jurisprudence requires the fact finder to credit unsupported assertions of an expert witness).

Another deficiency with Petitioner's argument is that it improperly attempts to incorporate by reference arguments made in Dr. Lidin's declaration into the Petition. Specifically, after asserting its argument regarding Folen's use of older equipment, Petitioner asserts "[f]or this *and the other reasons explained* in the Lid[i]n Declaration," an ordinary artisan would recognize Folen's peaks as teaching the claimed peaks at 17.5 and 19.7°2θ± 0.1°2θ. Pet. 40 (citing Ex. 1006 ¶ 38–42, 61–66, 71–75)

(emphasis added). According to our rules, however, "[a]rguments must not be incorporated by reference from one document into another document." 37 C.F.R. § 42.6(a)(3). To the extent the "other reasons" support Petitioner's contentions, we do not consider such arguments for purposes of our Decision.

Finally, Petitioner relies on the work of Dr. Kaduk as confirming that the psilocybin analyzed by Folen was consistent with a mixture of Polymorph A' with detectible amounts of Polymorph B and Hydrate A. Pet. 40 (citing Ex. 1008 ¶ 48). It is unclear how this helps Petitioner's argument, though, as Dr. Lidin testifies that Polymorph A of the '257 patent "actually is a mixture of Polymorph A-prime and Polymorph B." Ex. 1006 ¶ 36. Petitioner and its experts are silent as to how the presence of Hydrate A may affect the XRPD diffractogram of Folen and why that alone does not distinguish Folen's psilocybin from Polymorph A of the '257 patent.

Thus, having considered the arguments and evidence presented, we find Petitioner has failed to demonstrate that Folen (or any of the cited references) teaches or suggests the claimed peaks at 17.5 and 19.7°2θ ±0.1°2θ, as required by each of the challenged claims. Accordingly, we determine Petitioner has not shown that it is more likely than not that any of the challenged claims of the '257 patent are unpatentable as obvious over the cited references.

F. Enablement

Petitioner asserts that claims 1–23 of the '257 patent fail to meet the enablement requirement. Pet. 52–55. Under 35 U.S.C. § 112(a), the specification must enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). To determine whether undue experimentation

would be required, we may consider the following "*Wands* factors": (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.*

Petitioner asserts that because the claims require an "oral dosage form" and the Specification "does not teach how to analyze the claimed oral dosage form to determine whether the claimed characteristics of Polymorph A or its purity limitations are present (Claims 1-9, 15-16, 21), or to determine whether silicified microcrystalline cellulose ("SMCC") is present in the claimed particle size ranges (Claims 10-14, 17-20, 22-23)." Pet. 52–53. Petitioner argues that "polymorphic characterization of the claimed crystalline psilocybin in an oral dosage form is impossible when the peaks in the XRPD diffractogram of excipients may overlap or interfere with the peaks generated by the '257 Patent's claimed form of crystalline psilocybin." Pet. 53. Moreover, Petitioner argues that peaks generated by SMCC will interfere and likely make it impossible to detect the claimed peaks for Polymorph A. *Id.* (citing Ex. 1010 ¶¶ 54–59).

Petitioner further asserts that "it is not possible for a POSA to attribute *to the crystalline 'Polymorph A'* impurities that exist in a final drug product." *Id.* at 53–54 (citing Ex. 1010 ¶¶ 58, 60–62). Petitioner contends that the same reasoning applies to claims 7 and 8. *Id.* at 54 (citing Ex. 1010 ¶¶ 68–71).

Petitioner also argues that "the '257 Patent fails to enable a POSA how to ascertain the SMCC particle size ranges in an oral dosage form" because "[t]he size of ingredients in an oral dosage form change as a result

of the manufacturing process, and accurate measurement of the size of ingredients in a final oral dosage form is a known and notoriously challenging problem in the field which the '257 Patent does not purport to solve." *Id.* at 54–55 (citing Ex. 1010 ¶¶ 72, 73).

In response, Patent Owner contends that Petitioner's challenge fails "because Petitioner's arguments are premised on an incorrect interpretation of the law of enablement." Prelim. Resp. 27. Patent Owner argues that "[w]hether a claim is enabled has nothing to do with whether a particular claim element may be 'analyzed' or have its presence 'determined' as Petitioner alleges." *Id.* at 28. Patent Owner asserts that the '257 patent discloses how to make the claimed crystalline polymorph, the claimed oral dosage forms, and how to use the oral dosage forms. *Id.* at 28–29 (citing Ex. 1001, 17:15–18:67, 20:10–26, 21:31–22:13, 32:7–39, 66:47-69:20, Figs. 7a, 8a).

We agree with Patent Owner that Petitioner has not shown sufficiently that the claims lack enablement. Petitioner appears to argue that in order for the claims to be enabled, a person of ordinary skill in the art must be able to analyze the final dosage form to determine whether the recited attributes of Polymorph A and SMCC are present. Pet. 53. We do not read the claims so narrowly. The oral dosage form comprises "Polymorph A characterized by" the recited peaks, with a particular chemical purity, and further comprises SMCC with certain particle sizes. *See, e.g.*, Ex. 1001, claims 1, 10–14. In other words, the oral dosage form is made up of components with those attributes, which can be determined before preparing the oral dosage form.

The Specification is consistent with this interpretation, describing the development of the drug formulations with psilocybin, SMCC, and various excipients. For example, the Specification describes the experimental

procedure for preparing Polymorph A with the recited peaks as shown in Figure 7a and a chemical purity of 99.3%. *See* Ex. 1001, 32:7–39, Fig. 7a. Moreover, Example 12 of the Specification describes the formulation development and, in particular, the use of SMCC with varying particle sizes. *Id.* at 66:47–69:20; *see also id.* at 20:10–26. In light of the relatively high level of skill of those in the art and the Specification's detailed description—including working examples—of the preparation of Polymorph A and the development of the drug formulation with the specific particle sizes of SMCC, we are not persuaded that Petitioner has shown sufficiently that the '257 patent does not enable the claims.

G. Remaining Arguments

Patent Owner also argues we should deny the Petition for failure to identify all real parties-in-interest in the Petition. Prelim. Resp. 29–42. Because we determine that Petitioner has not sufficiently established that any of the challenged claims are unpatentable, we need not address that issue in this Decision.

III. CONCLUSION

For the foregoing reasons, we determine that Petitioner has failed to show it is more likely than not that any of the challenged claims of the '257 patent are unpatentable.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* as to all challenged claims of the '257 patent and no trial is instituted.

PETITIONER:

John M. Griem, Jr.
Theodore Y. McDonough
CARTER LEDYARD & MILBURN LLP
griem@clm.com
mcdonough@clm.com

PATENT OWNER:

Michael Tuscan
Jason C. Valentine
Adam Pivovar
COOLEY LLP
mtuscan@cooley.com
jvalentine@cooley.com
apivovar@cooley.com