

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

BAUSCH HEALTH IRELAND LIMITED,
Patent Owner.

IPR2022-01102
Patent 9,610,321 B2

Before SHERIDAN K. SNEDDEN, CYNTHIA M. HARDMAN, and
MICHAEL A. VALEK, *Administrative Patent Judges*.

SNEDDEN, *Administrative Patent Judge*.

DECISION

Denying Institution of *Inter Partes* Review

35 U.S.C. § 314

Granting Patent Owner's Motion to Seal and Enter Default Protective Order

37 C.F.R. §§ 42.14, 42.54

I. INTRODUCTION

A. *Background and Summary*

Mylan Pharmaceuticals, Inc. (“Petitioner”) filed a Petition requesting an *inter partes* review of claims 1–16 of U.S. Patent No. 9,610,321 B2 (“the ’321 patent,” Ex. 1001). Paper 2 (“Pet.”). Bausch Health Ireland Limited (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 7 (“Prelim. Resp.”).

To institute an *inter partes* review, we must determine that the information presented in the Petition shows “a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a) (2018). The Supreme Court has held that a decision to institute under 35 U.S.C. § 314 may not institute on less than all claims challenged in the petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018). After considering the evidence and arguments presented in the Petition, we determine that Petitioner has not demonstrated a reasonable likelihood of success in proving that claims 1–16 of the ’321 patent is unpatentable.

B. *Real Parties-in-Interest*

Petitioner identifies itself, Mylan Laboratories Ltd., Mylan Inc., and Viartis Inc. as real parties-in-interest. Pet. 3.

Patent Owner identifies itself and Salix Pharmaceuticals, Inc. as real parties-in-interest. Paper 3, 2.

C. *Related Matters*

Petitioner has filed petitions for *inter partes* review involving patents related to the ’321 patent in IPR2022-00722 (Patent 7,041,786); IPR2022-

01103 (Patent 9,616,097), IPR2022-01104 (Patent 9,919,024), and IPR2022-01105 (Patent 9,925,231). Pet. 4; Paper 3, 3–4.

The parties state that the '231 patent is involved in *Bausch Health Ireland Ltd. v. Mylan Laboratories Ltd.*, 1-22-cv-00020 (N.D. W.Va.); 2-21-cv-00573 (W.D. Pa. (administratively closed)); and *Bausch Health Ireland Ltd. v. MSN Laboratories Pvt. Ltd.*, 2-21-cv-10057 (D.N.J.). Pet. 4; Paper 3, 2–3. Patent Owner additionally identifies *Bausch Health Ireland Ltd. v. Mylan Laboratories Ltd.*, 1-21-cv-00611 (D. Del.) (closed), and 2:21-cv-10403 (D.N.J.) (transferred to N.D. W.Va.). Paper 3, 2–3.

D. The '321 patent (Ex. 1001)

The '321 patent, titled “Formulations of Guanylate Cyclase C Agonists and Methods of Use,” relates to pharmaceutical formulations containing guanylate cyclase-C (“GCC”) agonist peptides, including those described in U.S. Patent No. 7,041,786.¹ Ex. 1001, code (54), 1:30–32, 3:19–20, 7:15–16. According to the Specification, formulating “peptides for pharmaceutical delivery presents a number of special problems,” including chemical and physical stability problems due to the peptides degrading by a variety of mechanisms. *Id.* at 3:24–28.

The Specification describes exemplary pharmaceutical formulations containing “GCC agonist peptides formulated with one or more excipients such that the peptide is stabilized against chemical degradation.” *Id.* at 8:34–36. “The ideal excipient or combination of excipients will be non-hygroscopic, have few or no reducing sugars, and be substantially free of contaminants.” *Id.* at 8:39–42. Excipients may include carriers and lubricants. *Id.* at 9:33–65, 12:10–14, 13:3. One example formulation

¹ U.S. Patent No. 7,041,786 appears in this record as Shailubhai, Ex. 1005.

includes a GCC agonist peptide, an inert carrier, e.g., low-moisture microcrystalline cellulose (Avicel PH 112), and a lubricant, e.g., magnesium stearate. *Id.* at 18:13–30, 94:20–33 (Example 14).

The exemplary formulations include the GCC agonist peptide designated SP-304. *Id.* at 94:10. SP-304, also known as plecanatide, has the amino acid sequence shown in SEQ ID NO:1. *Id.* at 6:63–64, 7:21–25, 21:37, 23:20–23.

E. Representative Claims

Independent claims 1 and 3, reproduced below, are representative of the claims challenged in this proceeding.

1. A method for treating chronic constipation in a human subject comprising

orally administering to said human subject a composition consisting of a per unit dose of 3 mg or 6 mg of a peptide consisting of SEQ ID NO:1

wherein the peptide is a [4,12; 7,15] bicycle, an inert low moisture carrier, and a lubricant, and

wherein the peptide has a chromatographic purity of no less than 91% after storage for at least three months.

3. A method of treating or alleviating a symptom associated with chronic idiopathic constipation or irritable bowel syndrome in a human subject comprising

orally administering to said human subject a composition consisting of a per unit dose of 3 mg or 6 mg of a peptide consisting of SEQ ID NO:1

wherein the peptide is a [4,12; 7,15] bicycle, an inert low moisture carrier, and a lubricant, and

wherein the peptide has a chromatographic purity of no less than 91% after storage for at least three months.

Ex. 1001, 253:12–19, 23–30.

Challenged dependent claims 2, 5–7, and 11–13 depend directly or indirectly from claim 1. Challenged dependent claims 4, 8–10, and 14–16 depend directly or indirectly from claim 3.

F. Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–12 are unpatentable on the following four grounds:

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1	1–6, 8–9, 11–16	103(a)	Shailubhai, ² Camilleri, ³ Remington, ⁴ Mihranyan ⁵
2	7, 10	103(a)	Shailubhai, Camilleri, Remington, Mihranyan, Currie ⁶

² Shailubhai et al., U.S. Patent No. 7,041,786 B2, issued May 9, 2006 (“Shailubhai,” Ex. 1005).

³ Camilleri et al., *Challenges to the Therapeutic Pipeline for Irritable Bowel Syndrome: End Points and Regulatory Hurdles*, GASTROENTEROL., 135, 1877–1891 (2008) (“Camilleri,” Ex. 1031).

⁴ Rudnic, *Chapter 45: Oral Solid Dosage Forms*, in REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY 21st ed. (2005) (“Remington,” Ex. 1006).

⁵ Mihranyan et al., *Moisture Sorption by Cellulose Powders of Varying Crystallinity*, 269(2) Int. J. Pharm. 433–442 (2004) (“Mihranyan,” Ex. 1007).

⁶ Currie et al., *Methods and Compositions for the Treatment of Gastrointestinal Disorders*, U.S. Patent Publication No. 2005/0020811 (2005) (“Currie,” Ex. 1032).

Ground	Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
3	1–4, 11–16	103(a)	2009 Abstract, ⁷ Doelker ⁸
4	5–10	103(a)	2009 Abstract, Doelker, Currie

Pet. 6–7. Petitioner supports its contentions with the Declarations of Graham Buckton, Ph.D. (Ex. 1002, “Buckton Decl.”) and Uwe Christians, M.D., Ph.D. (Ex. 1004), among other evidence.

II. ANALYSIS

A. *Level of Ordinary Skill in the Art*

We consider the grounds of unpatentability in view of the understanding of a person of ordinary skill in the art at the time of the invention. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). Petitioner contends that as of September 15, 2011 (*see supra* n.1), a person of ordinary skill in the art (sometimes referred to herein as a “skilled artisan”) “had an M.D. with experience in treating constipation and related disorders.”

Pet. 11. “This individual could work with other specialists including, e.g., a formulator with the equivalent of a graduate degree in pharmaceuticals or a related field, and knowledge and experience making oral-dosage formulations, a clinical pharmacologist, and a medicinal chemist.” *Id.*

⁷ Shailubhai et al., SP-304 to Treat GI Disorders – Effects of a Single, Oral-Dose of SP-304 on Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Healthy Volunteers, 136(5) *Gastroenterol.* A641, Abstract W1041 (2009) (“2009 Abstract,” Ex. 1009).

⁸ Doelker et al., *Morphological, Packing, Flow and Tableting Properties of New Avicel Types*, 21(6) *Drug Dev. Ind. Pharm.* 643–661 (1995) (“Doelker,” Ex. 1010).

(citing Buckton Decl. ¶¶ 81–84). Patent Owner does not dispute Petitioner’s proposal. Prelim. Resp. 42–43.

Because Petitioner’s proposed level of ordinary skill in the art appears to be consistent with the cited prior art and is undisputed on this record, we adopt it for purposes of this Decision.

B. Claim Construction

In AIA proceedings 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). In particular, 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.*

Petitioner asserts that the claims do not require any construction, but also states that a person of ordinary skill in the art would have understood the term “inert low moisture carrier,” which appears in claim 1, to include Avicel PH112. Pet. 13. Patent Owner “does not challenge the claim construction positions set forth in the Petition.” *See generally* Prelim. Resp.

For purposes of this Decision, we determine that we need not construe any claim term. *See Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1375 (Fed. Cir. 2019) (“The Board is required to construe ‘only those terms . . . that are in controversy, and only 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)).

C. Obviousness: Legal Standard

A claim is unpatentable as obvious under 35 U.S.C. § 103(a) 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 said subject matter pertains. *See also KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007); 35 U.S.C. § 103(a) (2006). The question of obviousness is resolved based on 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) any objective indicia of nonobviousness. *Graham*, 383 U.S. at 17–18. An obviousness determination requires finding a reason to combine accompanied by a reasonable expectation of achieving what is claimed in the patent-at-issue. *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016). “[A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *KSR*, 550 U.S. at 419–20.

D. Overview of Asserted Prior Art

1. Shailubhai (Ex. 1005)

Shailubhai is a U.S. patent titled “Guanylate Cyclase Receptor Agonists for the Treatment of Tissue Inflammation and Carcinogenesis.” Ex. 1005, code (54), 1:14–22. Shailubhai issued on May 9, 2006, and thus is prior art to the challenged claims. *Id.* at code (45).

Shailubhai discloses peptide agonists of guanylate cyclase receptors and their use in treating gastrointestinal inflammatory disorders such as Crohn’s disease and ulcerative colitis. *Id.* at 4:43–61. Shailubhai discloses

that “[t]he most preferred peptide,” SP304,⁹ is “defined by SEQ ID NO:20” and “gave the greatest enhancement of intracellular cGMP of all the analogs tested.” *Id.* at 5:4–5, 15:57–58.

Shailubhai discloses that the peptides may be “formulated with various excipients,” and “may be administered in solutions, powders, suspensions, emulsions, tablets, capsules, transdermal patches, ointments, or other formulations” that are “made using methods well known in the art.” *Id.* at 5:24–26, 13:19–30. Shailubhai claims unit dose forms, selected from a tablet, capsule, solution, or inhalation formulation, comprising SP304 and one or more excipients. *Id.* at 37:4–6, 38:1–6 (claim 5).

2. *Remington (Ex. 1006)*

Remington, titled “The Science and Practice of Pharmacy,” is a “textbook and reference work for pharmacists, physicians, and other practitioners of the pharmaceutical and medical sciences.” Ex. 1006, i, iii. Remington was published in 2005, and thus is prior art to the challenged claims. *Id.* at iii.

Remington explains that “[d]rug substances most frequently are administered orally by means of solid dosage forms such as tablets and capsules.” *Id.* at 889. Tablets may be manufactured by direct compression, which “consists of compressing tablets directly from powdered material without modifying the physical nature of the material itself.” *Id.* at 901. Remington describes microcrystalline cellulose (“MCC,” sold under the brand name Avicel) as a common excipient in direct-compression

⁹ Petitioner contends, and Patent Owner does not dispute, that SP304 is also known as plecanatide. *See, e.g.*, Pet. 7, 22, 45.

formulations. *Id.* at 891. MCC is water-insoluble but can draw fluid into a tablet by capillary action. *Id.* at 903.

Remington also teaches that lubricants such as magnesium stearate “have a number of functions in tablet manufacture,” including that they “prevent adhesion of the tablet material to the surface of the dies and punches, reduce interparticle friction, facilitate the ejection of the tablets from the die cavity, and may improve the rate of flow of the tablet granulation.” *Id.* at 892.

3. *Mihranyan (Ex. 1007)*

Mihranyan, an article titled “Moisture sorption by cellulose powders of varying crystallinity,” describes a study designed “to investigate the influence of crystallinity and surface area on the uptake of moisture in cellulose powders.” Ex. 1007, 433. Mihranyan was published in 2004, and thus is prior art to the challenged claims. *Id.*

In its Introduction section, Mihranyan notes that MCC is one of the most common tableting excipients and states that “[o]rdinary MCC is manufactured with 4–5% (w/w) moisture content (European Pharmacopoeia, 2002). For moisture sensitive drugs, low moisture grades of MCC are available (1.5%, w/w, moisture in Avicel PH 112 and 3%, w/w, moisture in Avicel PH 103, FMC Corp.).” *Id.*

4. *2009 Abstract (Ex. 1009)*

The 2009 Abstract is titled “SP-304 to Treat GI Disorders - Effects of a Single, Oral-Dose of SP-304 On Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Healthy Volunteers.” Ex. 1009, A-641. The 2009 Abstract was published in 2009, and thus is prior art to the challenged claims. *Id.* at cover page.

SP-304 is “a synthetic analog of uroguanylin . . . that regulates ion and fluid transport in the GI tract.” *Id.* The 2009 Abstract describes a clinical trial wherein a single oral ascending dose of SP-304 was administered to healthy volunteers. *Id.*

5. *Doelker (Ex. 1010)*

Doelker is an article titled “Morphological, Packing, Flow and Tableting Properties of New Avicel Types.” Ex. 1010, 643. Doelker was published in 1995, and thus is prior art to the challenged claims. *Id.*

Doelker compares “classical” grades of Avicel MCC to new grades, including Avicel PH-112. *Id.* The products differ in their nominal particle size and moisture content. *Id.* Doelker determines the basic properties of the products, then evaluates their compactibility “and the effect of adding a hydrophobic lubricant (0.5% magnesium stearate) on the compact strength.” *Id.* Doelker explains that Avicel PH-112 has “the typical particle size specifications of Avicel PH-102 (100 μ m) but very low moisture content (max. 1.5%) which makes it an ideal excipient for moisture-sensitive substances.” *Id.* at 645. Doelker describes conventional grades of Avicel (with the exception of Avicel PH-103) as having too high water content for tablets containing water-sensitive drugs. *Id.*

6. *Camilleri (Ex. 1031)*

Camilleri is a review article, titled “Challenges to the Therapeutic Pipeline for Irritable Bowel Syndrome: End Points and Regulatory Hurdles.” Ex. 1031, 1877. Table 1 of Camilleri lists “[s]everal of the drugs in development that are in ongoing or planned clinical trials for [Irritable Bowel Syndrome (IBS)].” *Id.* Guanilib (plecanatide) is indicated as in a phase I clinical trial. *Id.* at 1878.

Camilleri additionally discloses linaclotide, a related GCC-agonist peptide, for treating both chronic constipation and IBS given its ability to increase intestinal water and electrolyte secretion in the GI tract. *Id.* at 1879, Table 2.

7. Currie (Ex. 1032)

Currie discloses linaclotide, the active ingredient of Linzess. Currie discloses administering GCC-agonist peptides for the treatment of IBS and chronic constipation. Ex. 1032 ¶¶ 41, 97. Currie also discloses co-administration with other therapeutic agents, including laxatives and cGMP phosphodiesterase inhibitors (e.g., motapizone, zaprinast, suldinac sulfone). *Id.* ¶ 11.

E. Ground 1: Alleged Obviousness over Shailubhai, Camilleri, Remington, and Mihranyan

For Ground 1, Petitioner asserts that claims 1–6, 8–9, and 11–16 are unpatentable as obvious over Shailubhai, Camilleri, Remington, and Mihranyan. Pet. 21–43. Patent Owner disputes Petitioner’s contentions. Prelim. Resp. 48–64.

On this record Petitioner has not shown a reasonable likelihood of establishing that at least one of the challenged claims is unpatentable as obvious over Shailubhai, Camilleri, Remington, and Mihranyan. We focus our analysis on the recitation of “an inert low moisture carrier” in the independent claims.

1. Brief Summary of Petitioner’s Arguments

Petitioner argues that treating chronic constipation by orally administering plecanatide to a human subject would have been obvious in view of Shailubhai and Camilleri, which in combination disclose administering an oral-dosage form of a GCC-agonist peptide consisting of

SEQ ID NO:1, where the peptide is a (4,12; 7,15) bicycle for the treatment of IBS with Constipation (IBS-C). Pet. 23–25 (citing Ex. 1005, 5:4–15, 10:66–67, 35:8–25; Ex. 1031, 1878; Ex. 1002 ¶¶ 518, 412–413; Ex. 1004 ¶¶ 51–56).

Petitioner also argues that a person of ordinary skill in the art would have had “good reason” to formulate “Shailubhai’s plecanatide, formulated consistent with Remington and Mihranyan, for treating chronic constipation” to arrive at the method recited in independent claims 1 and 3. Pet. 21–22 (claim 1), 37–38 (claim 3). In brief, Petitioner argues that Shailubhai teaches plecanatide can be formulated as a tablet, and Remington teaches that most commercialized tablets are compressed tablets. *Id.* at 27–28 (citing, e.g., Ex. 1005 (Shailubhai), 5:24–30; Ex. 1006 (Remington), 889, 891; Buckton Decl. ¶¶ 140–41; Ex. 1004 (Christians Decl.) ¶¶ 64–65). Petitioner further argues that a person of ordinary skill in the art would have had good reason to use MCC in the tablet, including because it was common excipient in compressed tablets, acts as both a carrier and binder, and is partially self-lubricating. *Id.* at 28 (citing, e.g., Buckton Decl. ¶ 101; Ex. 1006 (Remington), 891–92, 903; Ex. 1007 (Mihranyan), 433); *see also id.* at 15–17 (additionally citing, e.g., Ex. 1029 (Aulton), 136, Table 8.16, 302; Ex. 1008 (Excipients Handbook), 130).

Regarding the independent claims’ recitation of “an inert low moisture carrier,” Petitioner contends skilled artisans “routinely used low-moisture MCC,” such as the Avicel PH 112 taught in Mihranyan, “for moisture-sensitive materials.” *Id.* at 16–17 (citing, e.g., Ex. 1008 (Excipients Handbook), 132 (disclosing “[s]everal different grades” of MCC); Ex. 1007 (Mihranyan), 433); *id.* at 28 (additionally citing Buckton

Decl. ¶ 145); Ex. 1001, claims 1 and 3. Petitioner asserts that skilled artisans “recognized low-moisture MCC as a preferred inert carrier for direct-compression tableting of peptides” because “[p]eptides were generally understood to be susceptible to water-induced degradation.” *Id.* at 17 (citing Ex. 1016 (Lai), 489; Buckton Decl. ¶¶ 102, 104); *see also id.* at 28 (arguing that skilled artisans “had good reason to use a low-moisture MCC carrier (e.g., Mihranyan’s Avicel PH112) to reduce plecanatide’s moisture exposure from tablet excipients because peptides generally are subject to moisture-based degradation during storage”) (citing Buckton Decl. ¶¶ 143–44, 146–47; Ex. 1016 (Lai), 489; Ex. 1006 (Remington), 731); *see also* Pet. 37 (“The same combination discussed [with regard to claim 1] also rendered [claim 3] obvious.”).

2. Analysis

Petitioner has not shown a reasonable likelihood of prevailing on Ground 1, at least because Petitioner has not sufficiently shown that the cited prior art taught or suggested use of “an inert low moisture carrier,” as recited in independent claims 1 and 3.¹⁰

As an initial matter, we note that Petitioner does not cite any evidence suggesting that plecanatide was known to be a moisture-sensitive material. *See* Prelim. Resp. 3. Rather, Petitioner argues that “[p]eptides were generally understood to be susceptible to water-induced degradation.”

¹⁰ Claims 1 and 3 recite distinct methods of using the same composition. *See supra* I.E.; *see also* Pet. 37 (“Independent claim 3 differs from claim 1 only in the claim preamble.”). As our analysis primarily addresses the sufficiency of Petitioner’s challenge with regard to the recited composition, we focus, for brevity, our analysis on claim 1 given the relevant overlap in the scope and subject matter recited in independent claims 1 and 3.

Pet. 17; *see also id.* at 28 (“peptides generally are subject to moisture-based degradation during storage”). To support this contention, Petitioner cites Lai, Dr. Buckton’s testimony, and Remington. *See id.* at 17 (citing Ex. 1016 (Lai), 489; Buckton Decl. ¶¶ 102, 104); *see also id.* at 25–26 (additionally citing Buckton Decl. ¶¶ 143–44, 146–47; Ex. 1006 (Remington), 731).

Lai, a review article published in 1999, “summarizes the major chemical reactions affecting proteins and peptides in the solid-state” and discusses factors that influence these reactions, including “temperature, moisture content, excipients, and the physical state of the formulation (amorphous vs crystalline).” Ex. 1016 (Lai), Abstr. Petitioner and Dr. Buckton do not quote from Lai or indicate any specific portion of Lai that supports their positions beyond a bare citation to page 489. That page states, among other things, that “[f]actors that may impact the chemical stability of proteins and peptides in the solid-state include residual moisture and the excipient(s) used in a formulation.” *Id.* at 489.

On this record, we find that Petitioner’s reliance on Lai is insufficient to carry its burden for institution. Petitioner and Dr. Buckton generically cite Lai’s first page (page 489), but fail to articulate any specific reason why a skilled artisan would have been motivated to use a low-moisture MCC carrier in a peptide formulation (let alone in the claimed plecanatide formulation). At most, Lai page 489 is equivocal about the impact of moisture on peptides, stating only that, among other factors, moisture “*may* impact the chemical stability of proteins and peptides in the solid-state.” *Id.* (emphasis added). Neither Petitioner nor Dr. Buckton adequately explains how this teaching (or any other teaching in Lai) would have informed a

person of ordinary skill in the art that peptides were moisture-sensitive, thereby motivating use of a low-moisture MCC carrier.

To be sure, Lai page 489 teaches that moisture content is one of several factors (along with temperature, excipients, and the physical state of the formulation) that influences chemical reactions affecting peptides in the solid state. *Id.* at Abstr. But other evidence Petitioner cites reflects that moisture content is a factor that influences degradation of *all* drug formulations, whether they comprise small molecules or peptides. For example, in the context of drug formulations generally, Remington teaches that the “presence or absence of moisture is one of the most important environmental factors that can affect solid-state stability.” Ex. 1006 (Remington), 731; *see also* Buckton Decl. ¶ 143 (quoting same); Pet. 25–26 (citing same). Similarly, Aulton states: “In general, drug substances decompose as a result of the effects of heat, oxygen, light and moisture.” Ex. 1029 (Aulton), 9; *see also* Buckton Decl. ¶ 104 (citing same). Despite this global concern with moisture, the record does not suggest the use of low-moisture MCC in every tablet formulation, but rather only for moisture-sensitive drugs. *See* Ex. 1007 (Mihranyan), 433 (“Ordinary MCC is manufactured with 4-5% (w/w) moisture content,” but “[f]or moisture sensitive drugs, low moisture grades of MCC are available.”); Ex. 1010 (Doelker), 660 (“Avicel PH-112 is indicated for moisture-sensitive drugs”). Petitioner has not sufficiently shown that one of ordinary skill in the art would have understood plecanatide, or GCC agonist peptides more generally, to be moisture-sensitive drugs.

Indeed, various portions of Lai not cited by Petitioner undercut Petitioner’s blanket assertion that the ordinarily skilled artisan would have

understood that “peptides generally are subject to moisture-based degradation during storage.” Pet. 28. First, Lai recognizes that as compared to the solid-state stability of small molecules, the effect of moisture “on the solid state chemical stability of proteins and peptides [is] not as widely reported or understood.” Ex. 1016 (Lai), 493; *see also* Prelim. Resp. 3, 54. Second, although Lai states that “[r]esidual moisture is often thought to be responsible for protein and peptide chemical instability in the solid-state” (Ex. 1016 (Lai), 494), it also “describes instances in which peptides are *less stable* at lower moisture contents” (Prelim. Resp. 54–55 (citing Ex. 1016 (Lai), 492, 494)). Indeed, Lai reports instances in which solid state degradation “is accelerated in the low moisture range” (Ex. 1016, 492), conditions in which “residual water . . . can suppress a chemical reaction” that might otherwise cause degradation (*id.* at 494), as well as “other types of chemical instabilities” that exhibit a “bell-shaped relationship between degradation kinetics and moisture content” (*id.*). Thus, Lai suggests that moisture may have a variety of effects depending on the peptide and the circumstances of its formulation.

Given Lai’s more nuanced teachings about the varying effects of moisture (which Petitioner does not address), coupled with Petitioner’s unexplained, superficial citation to Lai, Petitioner does not sufficiently demonstrate for purposes of institution that a skilled artisan would have understood plecanatide to be a moisture-sensitive material such that they would have been motivated to formulate it with a low-moisture MCC carrier. *See, e.g., Novartis Pharm. Corp. v. Watson Labs., Inc.*, 611 F. App’x 988, 995–96 (Fed. Cir. 2015) (affirming finding of no motivation to add an antioxidant to a formulation where the prior art did not

unambiguously identify the subject drug as susceptible to oxidative degradation). A petition must include “a *detailed explanation of the significance of the evidence.*” 37 C.F.R. § 42.22(a)(2) (emphasis added); *see also* 35 U.S.C. § 312(a)(3) (petition must identify “*with particularity . . . the evidence that supports the grounds for the challenge to each claim*”) (emphasis added). Here, the Petition fails to sufficiently explain how Lai supports Petitioner’s assertion that “[p]eptides were generally understood to be susceptible to water-induced degradation,” particularly given the equivocal and sometimes contrary teachings in Lai that the Petition ignores. Pet. 17.

Dr. Buckton’s testimony does not provide the missing explanation. He merely repeats the Petition’s statement that Lai teaches “peptides in particular are generally subject to degradation from moisture during storage,” without explaining how Lai supports that conclusion. Buckton Decl. ¶ 104; *see also id.* ¶ 144. Dr. Buckton also cites Aulton, but again fails to indicate exactly what in Aulton indicates that peptides generally, much less plecanatide specifically, are moisture-sensitive. *Id.* ¶ 144. Indeed, the cited page of Aulton does not mention peptides at all. *See* Ex. 1029 (Aulton), 9. On this record, Dr. Buckton’s testimony lacks sufficient explanation and is not persuasive to support Petitioner’s burden for institution. *See* 37 C.F.R. § 42.65(a) (“Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.”); *Verlander v. Garner*, 348 F.3d 1359, 1371 (Fed. Cir. 2003) (noting that Board has discretion to accord little weight to expert’s “broad conclusory statements that it determined were unsupported by corroborating references”).

For at least the reasons discussed above, on this record we are not persuaded that Petitioner has shown a reasonable likelihood of establishing that claim 1 is unpatentable as obvious over Shailubhai, Camilleri, Remington, and Mihranyan. Dependent claims 2, 4–6, 8–9, and 11–16 incorporate all of the limitations of independent claims 1 and 3. Petitioner’s arguments and evidence for these dependent claims do not remedy the deficiencies discussed above for claims 1 and 3. *See* Pet. 36–43. Accordingly, Petitioner has not demonstrated a reasonable likelihood of prevailing on Ground 1.

F. Ground 3: Alleged Obviousness over 2009 Abstract and Doelker

For Ground 3, Petitioner asserts that claims 1–4 and 11–16 are unpatentable under 35 U.S.C. § 103(a) as obvious over the 2009 Abstract and Doelker. Pet. 44–60. Patent Owner disputes Petitioner’s contentions. Prelim. Resp. 65–72.

On this record Petitioner has not shown a reasonable likelihood of establishing that at least one of the challenged claims is unpatentable as obvious over the 2009 Abstract and Doelker. We again focus our analysis on the recitation of “an inert low moisture carrier” in independent claims 1 and 3.

1. Brief Summary of Petitioner’s Arguments

Petitioner argues that a person of ordinary skill in the art “had good reason and reasonable expectation of success for administering 2009 Abstract’s peptide, formulated as Doelker taught, for treating chronic constipation.” Pet. 45. In brief, Petitioner argues that the 2009 Abstract teaches oral administration of SP-304 (plecanatide) for treating chronic constipation, while Doelker teaches direct-compression tablets consisting of

the inert low-moisture carrier Avicel PH112 and the lubricant magnesium stearate. *See, e.g.*, Pet. 46, 49–50. Petitioner reiterates its argument from Ground 1 that a person of ordinary skill in the art would have had “good reason to use a low-moisture MCC carrier (e.g., Doelker’s Avicel PH112) to reduce plecanatide’s moisture exposure from tablet excipients because peptides generally are subject to moisture-based degradation during storage.” *Id.* at 49 (citing Buckton Decl. ¶¶ 236–38, 561; Ex. 1016 (Lai), 489; Ex. 1006 (Remington), 731); *see also id.* at 17 (arguing that “[p]eptides were generally understood to be susceptible to water-induced degradation” and that skilled artisans “recognized low-moisture MCC as a preferred inert carrier for direct-compression tableting of peptides”) (citing Ex. 1016 (Lai), 489; Buckton Decl. ¶¶ 102, 104).

2. Analysis

For the same reasons discussed above for Ground 1, Petitioner has not sufficiently shown that the cited prior art taught or suggested use of “an inert low moisture carrier,” as recited in claims 1 and 3. Petitioner relies on the same rationale already discussed above, namely that a person of ordinary skill in the art “had good reason to use a low-moisture MCC carrier . . . because peptides generally are subject to moisture-based degradation during storage,” and cites the same evidence in support, namely Lai, Dr. Buckton’s testimony¹¹, and the general proposition that “moisture is

¹¹ For the proposition that “peptides generally are subject to moisture-based degradation during storage,” Petitioner cites different paragraphs of Dr. Buckton’s Declaration for Grounds 1 and 3. *See* Pet. 25 (citing ¶¶ 143, 144 for Ground 1), 47 (citing ¶¶ 236–238 for Ground 3). The citation to different paragraphs in the different grounds is immaterial to our analysis, because the paragraphs regarding the alleged moisture-based degradation of

one of the most important environmental factors that can affect solid-state stability.” Pet. 49 (quoting Ex. 1006 (Remington), 731).

Petitioner’s arguments and evidence are not sufficient for institution for the same reasons discussed above for Ground 1. *See supra* Section II.E.2. Petitioner’s arguments and evidence for dependent claims 2, 4, and 11–16 do not cure the deficiencies discussed above for independent claims 1 and 3. *See* Pet. 56–60. Accordingly, Petitioner has not demonstrated a reasonable likelihood of prevailing on Ground 3.

G. Grounds 2 and 4

For Grounds 2 and 4, Petitioner respectively asserts that (1) dependent claims 7 and 10 are unpatentable as obvious over Shailubhai, Camilleri, Remington, Mihranyan, and Currie; and (2) dependent claims 5–10 are unpatentable as obvious over the 2009 Abstract, Doelker, and Currie. Pet. 44, 61–63.

These grounds add Currie to reach additional limitations of the challenged dependent claims, but do not cure the deficiencies discussed above for Petitioner’s arguments for independent claims 1 and 3. Accordingly, Petitioner has not demonstrated a reasonable likelihood of prevailing on Grounds 2 and 4.

III. PATENT OWNER’S MOTION TO SEAL
AND ENTER DEFAULT PROTECTIVE ORDER

Patent Owner filed a Motion to Seal and Enter Default Protective Order. Paper 9. Patent Owner requests that we seal the entirety of Exhibit 2013 (excerpts of Patent Owner’s New Drug Application 208745), and the

peptides offer the substantially the same opinion and cite the same supporting evidence. *Compare* Buckton Decl. ¶ 144 *with id.* ¶ 236.

portions of Patent Owner's Preliminary Response (on pages 10, 32–34, and 60–61) that describe the content of Exhibit 2013. *Id.* at 3. Patent Owner has submitted a public version of its Patent Owner's Preliminary Response, wherein the information sought to be sealed is redacted. Patent Owner also requests entry of the Board's default protective order. *Id.* Petitioner does not oppose the motion. *Id.* at 1.

We find that Patent Owner has established good cause to seal its confidential information, and thus we grant its Motion to Seal. *See id.* at 3; 37 C.F.R. § 42.14. We also grant Patent Owner's request for entry of the Board's default protective order, but we note that Patent Owner did not make a copy of the default protective order of record. 37 C.F.R. § 42.54. We direct Patent Owner to file a copy of the Board's default protective order as an exhibit in this proceeding within five business days of this Decision.

We remind the parties that confidential information that is subject to a protective order ordinarily becomes public forty-five days after denial of a petition to institute. *See* 2019 Office Consolidated Trial Practice Guide,¹² 21–22. There is an expectation that information will be made public where the existence of the information is referred to in a decision to grant or deny a request to institute a review. *Id.* at 22. A party seeking to maintain the confidentiality of information, however, may file a motion to expunge the information from the record prior to the information becoming public. *Id.*; 37 C.F.R. § 42.56.

IV. CONCLUSION

After considering the evidence and arguments of record, we determine that Petitioner has not demonstrated a reasonable likelihood of prevailing

¹² Available at <https://www.uspto.gov/TrialPracticeGuideConsolidated>.

with respect to any claim challenged in the Petition.¹³ Accordingly, we do not institute an *inter partes* review.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* as to all challenged claims, and no trial is instituted;

ORDERED that Patent Owner's Motion to Seal and Enter Default Protective Order is *granted*; and

ORDERED that, within five business days of the entry of this Decision, Patent Owner shall file as an exhibit a copy of the Board's default protective order.

¹³ Because we deny the Petition on the merits, we do not reach Patent Owner's argument for discretionary denial under 35 U.S.C. § 325(d). Prelim. Resp. 23–41.

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