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Paper No. 7
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARGENTUM PHARMACEUTICALS LLC,
Petitioner

v.

MERCK PATENTGESELLSCHAFT,
Patent Owner

Case IPR2018-00423
Patent 8,673,921 B2

Before SUSAN L.C. MITCHELL, ROBERT A. POLLOCK, and RICHARD J. SMITH, *Administrative Patent Judges.*

SMITH, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314(a)

I. INTRODUCTION

Argentum Pharmaceuticals LLC ("Petitioner") filed a Petition (Paper 2, "Pet.") to institute an *inter partes* review of claims 1, 11, 12, 14, and 15 of U.S. Patent 8,673,921 (the "'921 patent"). 35 U.S.C. § 311. Merck Patentgesellschaft ("Patent Owner") filed a Preliminary Response to the Petition (Paper 6). ("Prelim. Resp.").

We have authority to determine whether to institute an *inter partes* review under 35 U.S.C. § 314. Based on the particular circumstances of this case, we exercise our discretion under 35 U.S.C. § 325(d) and do not institute *inter partes* review of the challenged claims.

A. Related Proceedings

Petitioner identifies the '921 patent as being the subject of the following proceedings: *Forest Laboratories, Inc. v. InvaGen Pharm. Inc.*, Civ. Action No. 15-cv- 272; *Forest Laboratories, Inc. v. Alembic Pharm. Ltd.*, Civ. Action No. 15-cv-273; *Forest Laboratories, Inc. v. Apotex Inc.*, Civ. Action No. 15-cv-274; *Forest Laboratories, Inc. v. Teva Pharm. USA Inc.*, Civ. Action No. 15-cv-275; *Forest Laboratories, Inc. v. InvaGen Pharm. Inc.*, Civ. Action No. 15-cv-277; and *Forest Laboratories, Inc. v. InvaGen Pharm. Inc.*, Civ. Action No. 15-cv-1078. Pet. 1–2. Patent Owner indicates that the above Civ. Action Nos. 272, 273, 274, 275, 277, and 1078 are now closed, and consolidated into *Forest Laboratories, LLC v. Accord Healthcare, Inc.*, Civ. Action No. 15-cv-272-GMS (consolidated) (D. Del. 2015). Paper 3, 2–3.

B. The '921 Patent

The '921 patent relates to "new crystalline modifications of the hydrochloride of 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine." Ex. 1001, Abstract; *see also id.* at Title (referencing "Polymorphic

Forms" of same compound). The '921 patent states that "[m]ethods for preparing pure crystals of 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine hydrochloride [vilazodone hydrochloride (VHCl)] have now been found." *Id.* at 2:25–27. The '921 patent further states that the morphologic Forms of 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine hydrochloride and dihydrochloride (Forms I–XI and XIII–XVI) are referred to as the "products of the invention" and can be used to treat and prevent a number of disorders. *Id.* at 14:58–15:19. The '921 patent also indicates that "[t]he present invention further provides pharmaceutical compositions or medicaments comprising a Product of the Invention." *Id.* at 15:22–26.

C. Illustrative Claims

Petitioner challenges claims 1, 11, 12, 14, and 15 of the '921 patent, of which claims 1 and 11 are the only independent claims. Claims 1 and 11 are reproduced below:

> 1. A compound which is 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine hydrochloride in its crystalline modification, wherein the compound is an anhydrate, hydrate, solvate or dihydrochloride.

Ex. 1001, 27:13–16.

> 11. A pharmaceutical composition comprising a compound which is 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine hydrochloride anhydrate in its crystalline modification IV, and one or more conventional auxiliary substances and/or carriers.

Id. at 28:5–9.

Claims 12 and 14 generally recite a method of treating certain disorders comprising administering the composition of claim 11 or a compound of claim 1, respectively. Ex. 1001, 28:10–20; 34–44. Claim 15 recites a "pharmaceutical

composition comprising a compound according to claim 1, and one or more conventional auxiliary substances and/or carriers." *Id.* at 28:45–47.

According to Patent Owner, the challenged claims "relate to crystalline vilazodone hydrochloride including vilazodone hydrochloride Form IV." Prelim. Resp. 1. Vilazodone hydrochloride is the active ingredient in VIIBRYD®, which is indicated for the treatment of major depressive disorder. *Id.* at 3–4; Ex. 2019, 1, 21. As set forth in the product labeling, "VIIBRYD tablets for oral administration contain polymorph Form IV vilazodone hydrochloride (HCl), a selective serotonin reuptake inhibitor and a $5HT_{1A}$ receptor partial agonist." Ex. 2019, 10.

D. The Asserted Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable under 35 U.S.C. §§ 102(b) and 103(a) based on the following grounds. Pet. 3.

Reference[s]	**Basis**	**Claims challenged**
'241 patent[1] as characterized by Patent Owner's Admissions[2]	§ 102(b)	1, 14, and 15
'241 patent, as characterized by Patent Owner's Admissions, in view of Bartoszyk[3]	§ 103(a)	1, 14, and 15

[1] Böttcher et al., U.S. Patent No. 5,532,241, issued July 2, 1996 ("'241 patent"). Ex. 1004.
[2] In referring to the term "Patent Owner's Admissions," Petitioner states that "[t]he background section of the '921 patent makes several admissions" Pet. 4–5. *See* Section II.C.2 *infra*.
[3] Bartoszyk et al., WO 00/72832 A2, published Dec. 7, 2000 ("Bartoszyk"). Ex. 1005.

Reference[s]	Basis	Claims challenged
'241 patent, as characterized by Patent Owner's Admissions, in view of Pavia[4] and Byrn[5]	§103(a)	1 and 11
'241 patent, as characterized by Patent Owner's Admissions, in view of Bartoszyk, Pavia, and Byrn	§103(a)	1, 12, 14, and 15

Petitioner also relies on the Declarations of Dr. Robin D. Rogers, Ph.D. (Ex. 1002), Dr. Sanjay J. Mathew, M.D. (Ex. 1003), and Dr. Gabriela Gurau, Ph.D. (Ex. 1039).

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that a "person of ordinary skill in the art ('POSA') at the time of the alleged invention of the '921 patent would have at least a bachelor's degree in chemistry, pharmaceutical sciences, or related discipline, and several years of experience working in pharmaceutical solid product development and/or solid-state chemistry." Pet. 11. Petitioner further states that "[t]he POSA would have expertise and experience in synthesis, crystallization, and characterization of salts and polymorphic forms. A POSA could have a lower level of formal education if such a person had a higher degree of relevant working experience." *Id.* at 11–12.

[4] Donald L. Pavia et al., *Introduction to Organic Laboratory Techniques: A Contemporary Approach*, 3rd ed., 508–540 (1988) ("Pavia"). Ex. 1032.
[5] Stephen R. Byrn et al., *Solid-State Chemistry of Drugs*, 2nd ed., 1–219 (1999) ("Byrn"). Ex. 1012.

Petitioner also states that a POSA "would collaborate with others having expertise in methods of treating mood disorders, including depression," and that such a POSA "would have an M.D. with extensive experience in the study and treatment of mood disorders. A POSA would understand the references referred to herein and would be able to draw inferences from them." *Id.* at 12.

According to Patent Owner, a POSA of the '921 patent "would have had at least a bachelor's degree in chemistry, pharmaceutical sciences, or a related discipline, along with several years of experience working in pharmaceutical solid product development and/or solid-state chemistry." Prelim. Resp. 9. Patent Owner also contends that a POSA "also would have had knowledge and experience (and/or access to others with knowledge and experience) in treating patients for depression or other conditions identified in the '921 patent and evaluating the effects of such treatment." *Id.*

Patent Owner acknowledges, and we agree, that Patent Owner sets forth a similar definition of a POSA as advanced by Petitioner. *Id.* However, Patent Owner states that Petitioner's identification of a POSA as including an individual having an "M.D. with extensive experience in the study and treatment of mood disorders" is flawed "because it does not require any experience in solid-state chemistry, which is the primary focus of the '921 patent claims." *Id.*

On this record and at this stage of the proceeding, we do not discern an appreciable difference in the parties' respective definitions of a person of ordinary skill in the art. Accordingly, we find that a person of ordinary skill in the art would have (1) at least a bachelor's degree in chemistry, pharmaceutical sciences, or related discipline, and several years of experience working in pharmaceutical solid product development and/or solid-state chemistry, and (2) expertise and experience in synthesis, crystallization, and characterization of salts and polymorphic forms.

We also find that a POSA could have a lower level of formal education if such a person had a higher degree of relevant working experience, and may have knowledge and experience (and/or access to others with knowledge and experience) in treating patients with mood disorders.

We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *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)).

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). "Under a broadest reasonable interpretation, words of the claim must be given their plain meaning, unless such meaning is inconsistent with the specification and prosecution history." *Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner states that "[t]he broadest reasonable interpretation of the term 'crystalline modification' is 'crystalline form.'" Pet. 9. Petitioner also states that "[t]he broadest reasonable interpretation of 'administering' is 'delivering into the body' of a patient." *Id.* at 11. Petitioner contends that such constructions are

consistent with the plain or ordinary meanings of the terms, and identical to constructions proposed by Patent Owner in district court litigation regarding the '921 patent. *Id.* at 9, 11. Patent Owner does not contest those proposed constructions, and notes that "[f]or purposes of this preliminary response, Patent Owner does not advance constructions for any other terms in the challenged claims." Prelim. Resp. 10. Accordingly, for purposes of this decision, we adopt the constructions that "crystalline modification" means "crystalline form," and that "administering" means "delivering into the body" of a patient.

Petitioner further argues that the terms "crystalline" and "crystalline modification"

> should not be interpreted to mean that Forms I to XVI must be "entirely crystalline" and no particular level of purity should be attributed to the crystalline compound recited in claims 1, 11, 12, 14, and 15. There is no support in the claims, specification, or prosecution history to support such a construction. Indeed, neither the claim terms nor the specification of the '921 patent mentions the purity of the crystalline compound recited in claims 1, 11, 12, 14, and 15.

Pet. 10.

Petitioner supports that argument by referencing the '921 patent generally and by citing a paragraph in the Rogers Declaration that purports to construe claims 1 and 11 as not excluding the possibility that "the crystalline modification is present in a mixture with the amorphous form and/or the free base or other crystalline forms." Ex. 1002 ¶ 47. However, paragraph 47 of the Rogers Declaration does not sufficiently or persuasively address the specific wording of claims 1 and 11 as a whole, and only refers generally to the '921 specification and claims. *See id.* ("neither the '921 patent specification [nor] the claims of the '921 patent require or specify any level of purity.") Furthermore, although experts may address underlying factual matters ("evidentiary underpinngs") when appropriate,

the ultimate issue of claim construction is a question of law. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S.Ct. 831, 841 (2015) ("'[e]xperts may be examined to explain terms of art, and the state of the art, at any given time,' but they cannot be used to prove 'the proper or legal construction of any instrument of writing.'") (citations omitted). Here, Petitioner relies on the conclusory statements of Dr. Rogers as purportedly establishing that the construction or scope of claims 1 and 11 does not exclude the possibility that "the crystalline modification is present in a mixture with the amorphous form and/or the free base or other crystalline forms." *See* Pet. 10; Ex. 1002 ¶ 47. Because "the ultimate question of construction [] remain[s] a legal question," *Teva*, 135 S.Ct. at 842, we provide our construction of claims 1 and 11 below.

Petitioner also argues that "[w]hen a patent recites a *compound comprising* a specific polymorphic form, that recitation does not foreclose the possibility that other active ingredients are also present" (Pet. 10 (emphasis added)). In support of this position, Petitioner relies on a district court decision[6] and a Board decision[7] on appeal from an Examiner's rejection, both of which were decided on their own facts and neither of which are binding on the Board. *See id.* Moreover, although claims 11 and 15 recite a "composition comprising," none of the challenged claims recite a "compound comprising." Ex. 1001, 27:13–16; 28:5–47.

Petitioner's argument and conclusory statements are not a sufficient showing to support a claim construction as proposed by Petitioner. Here, the specification of the '921 patent discusses the '241 patent and describes a "former" vilazodone hydrochloride that was a "mixture" of amorphous vilazodone hydrochloride,

[6] *In re Armodafinil Patent Litig., Inc.*, 939 F.Supp. 2d 456, 474 (D. Del. 2013).
[7] *Ex Parte Reddy*, 2010 Pat. App. LEXIS 13975, at *9–10 (BPAI March 31, 2010).

"crystallized" vilazodone hydrochloride, and the free base vilazodone hydrochloride, followed by the statement that "[*c*]*ertain crystalline, i.e. morphological forms* of pharmaceutical compounds may be of interest to those involved in the development of a suitable dosage form." Ex. 1001, 1:35–48; 1:65–2:21 (emphasis added). That background discussion in the '921 patent is followed immediately by the "Summary of the Invention" that begins with "[m]ethods for preparing *pure* crystals of [vilazodone hydrochloride] have now been found," followed by a description of fifteen crystalline forms (I–XI and XIII–XVI). *Id.* at 2:25–40 (emphasis added). The '921 patent further states that "[g]enerally, the specific crystalline forms of the present invention have certain advantages over the product obtained according to the ['241 patent]." *Id.* at 5:4–6. A fair reading of the specification of the '921 patent thus suggests that it is directed to the crystalline forms that vilazodone hydrochloride can take rather than a compound that is a mixture of crystallized vilazodone hydrochloride in combination with amorphous, and/or free base forms. However, Petitioner provides no persuasive analysis of whether or how its proposed interpretation is reasonable "in light of the specification." *See* 37 C.F.R. § 42.100(b).

Petitioner also fails to sufficiently analyze the claims as a whole to support its proffered interpretation of "crystalline" and "crystalline modification." Although the challenged claims do not expressly recite that the compound "in its crystalline modification" is "entirely" crystalline or a specific level of purity of the compound, that is not the end of the inquiry. *See Kyocera Wireless Corp. v. International Trade Commission*, 545 F.3d 1340, 1347 (Fed. Cir. 2008) (claim terms are not interpreted "in a vacuum, devoid of the context of the claim as a whole.") (citing cases). We also note that independent claims 1 and 11 recite a compound "which is" vilazodone hydrochloride in its crystalline modification

(claim 1) and "which is" vilazodone hydrochloride anhydrate in its crystalline modification IV (claim 11). Ex. 1001, 27:13–16; 28:5–9. Petitioner provides no interpretation of the transitional phrase "which is" in light of the specification. *See Lampi Corp. v. American Power Prods., Inc.*, 228 F.3d 1365, 1376 (Fed. Cir. 2000) ("Transitional phrases . . . must be interpreted in light of the specification to determine whether open or closed language is intended.") (citations omitted).

In view of the language of the specification discussed above and claim 1 as a whole, we find that the phrase "which is" as used in claim 1 is more akin to the closed term "consisting of" than the open term "comprising."[8] *See AFG Indus., Inc. v. Cardinal IG Co., Inc.* 239 F.3d 1239, 1245 (Fed. Cir. 2001) ("[C]losed transition phrases such as 'consisting of' are understood to exclude any elements, steps, or ingredients not specified in the claim.") (citations omitted); *CIAS, Inc. v. Alliance Gaming Corp.*, 504 F.3d 1356, 1360 (Fed. Cir. 2007) ("In the patent claim context, the term 'comprising' is well understood to mean 'including but not limited to.'") (citations omitted).

Accordingly, on this record, we construe claim 1 as limited to a compound which is vilazodone hydrochloride in its crystalline modification or form, wherein the compound is an anhydrate, hydrate, solvate, or dihydrochloride. Ex. 1001, 27:13–16. Claim 11 also uses the phrase "which is" as addressed above in connection claim 1, but claim 11 recites a "pharmaceutical composition comprising." *Id.*, 28:5–9. Thus, on this record, we construe claim 11 as a pharmaceutical composition that includes at least a compound which is vilazodone

[8] We also note that, in district court litigation regarding the '921 patent, neither Patent Owner nor Defendants sought to construe "crystalline modification" of vilazodone as referring to a form a vilazodone that is not crystalline. Ex. 2013, 3, n.6.

hydrochloride anhydrate in its crystalline modification (or form) IV, "and one or more conventional auxiliary substances and/or carriers," but the composition is not limited to those ingredients. *Id.*

In summary, for purposes of our decision herein, we adopt the constructions of independent claims 1 and 11 as set forth above, but we decline to further interpret "crystalline" or "crystalline modification" as proposed by Petitioner in view of the insufficient showing by Petitioner that such interpretation is proper.[9]

C. Anticipation by the '241 patent as characterized by Patent Owner's Admissions

Petitioner asserts that claims 1, 14, and 15 are anticipated by the '241 patent as characterized by Patent Owner's Admissions. Pet. 17–23. For the reasons set forth below, we exercise our discretion to decline institution because the same or substantially the same prior art or arguments were previously presented to the Office. *See* 35 U.S.C. § 325(d) ("In determining whether to institute or order a proceeding under this chapter . . . the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office."). When a prior art reference, such as the '241 patent, is presented in a petition and was already considered substantively by the Examiner, "the petitioner has the initial burden to identify [any] errors made by the examiner with respect to the prior art reference." *Neil*

[9] Petitioner has the burden of establishing a reasonable likelihood that it would prevail in showing the unpatentability of a challenged claim. 35 U.S.C. § 314(a).

Ziegmann, N.P.Z., Inc. v. Carlis G. Stephens, Case IPR2015-01860, slip op. at 10 (PTAB Sept. 6, 2017) (Paper 13).[10]

1. The '241 patent (Ex. 1004)

The '241 patent discloses 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine, its physiologically acceptable salts, a process by which it/they can be prepared, and their use in treating certain medical disorders. Ex. 1004, 7:30–58; Ex. 1001, 1:35–40. Example 4 of the '241 patent describes the preparation of 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine hydrochloride (VHCl). Ex. 1004, 11:17–24; Ex. 1001, 1:42–44. The '241 patent also discloses a composition that comprises a disclosed compound and a pharmaceutically acceptable carrier. Ex. 1004, 18:12–14. The '241 patent further discloses that its described compounds can be used for treating disorders such as depression, side-effects in the treatment of hypertension, and pre-menstrual syndrome. *Id.* at 8:24–38.

2. Patent Owner's Admissions

Petitioner describes four "admissions" regarding the '241 patent that it contends appear in the background section of the '921 patent. Pet. 4–5. According to Petitioner, those admission are as follows:

1. The '241 patent teaches 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine ("vilazodone") and its physiologically acceptable salts;

[10] This Decision on Request for Rehearing was before an expanded panel that included Chief Administrative Patent Judge David P. Ruschke and Deputy Chief Administrative Patent Judge Scott R. Boalick.

2. Example 4 of the ’241 patent teaches how to make vilazodone hydrochloride (“VHCl”), and that the product achieved is a mixture of crystalline HCl salt, amorphous HCl salt, and free base;

3. The product of Example 4 of the ’241 patent was a mixture of crystalline VHCl, amorphous VHCl, and vilazodone free base;[11] and

4. The ’241 patent discloses the use of VHCl in treating certain medical disorders. *Id.*

Patent Owner contests both the factual and legal basis for characterizing the asserted statements in the background section of the ’921 patent as “admissions,” particularly with respect to Petitioner’s contention that Example 4 of the ’241 patent is a mixture of crystalline, amorphous, and free base vilazodone hydrochloride. Prelim. Resp. 21–27; *see id.* at 22 (“the ’241 patent never describes or teaches crystalline vilazodone hydrochloride”).

On this record, and solely for purposes of our decision herein, we find that the above four “admissions” reasonably characterize the ’241 patent, and that the ’241 patent would have been so understood by the Examiner, based on the disclosures of the ’241 patent and the specification of the ’921 patent, and the Examiner’s statement of reasons for allowance. But to be clear, because we find that the four “admissions” reasonably characterize the teachings of the ’241 patent, we need not find and do not find that the above four statements are admissions by Patent Owner. Any reference herein to “Patent Owner’s Admissions” should only

[11] Petitioner’s Declarant, Dr. Rogers, acknowledges that “neither the [Patent Owner’s Admissions] of the ’921 patent nor Example 4 of the ’241 patent indicate how much amorphous VHCl or vilazodone free base is present in the mixture.” Ex. 1002 ¶ 142.

be understood as a reference to those four statements advanced by Petitioner and not as "admissions."

3. Prosecution History

The specification of the '921 patent discusses the '241 patent, and distinguishes the '241 patent from the disclosed invention. *See, e.g.*, Ex. 1001, 1:35–41; 5:4–6.

During the prosecution of the '921 patent, a set of claims was submitted in a Preliminary Amendment,[12] and allowed without a rejection. Ex. 2012, 1–6; Pet. 7; Prelim. Resp. 8. The Examiner issued a Notice of Allowability that stated:

> 4. The following is an examiner's statement of reasons for allowance: The instantly claimed crystalline compounds, compositions, and methods for using the same, are novel and non-obvious over the prior art. The closest prior art is U.S. Patent no. 5,532,241, which does not teach the claimed crystalline forms. This reference does not encompass the scope of the instant application. This reference lacks identical or obvious crystalline forms of 1-[4-(5-cyanoindol-3-yl)butyl]-4-(2-carbamoyl-benzofuran-5-yl)-piperazine. A person of ordinary skill in the art would not have expected that making modifications would retain identical activity as disclosed in the prior art.

Ex. 1006, 8.

4. Analysis

When evaluating whether to exercise our discretion when the same or substantially the same prior art or arguments were previously presented to the Office under § 325(d), the Board has weighed several non-exclusive factors,

[12] The claims in the Preliminary Amendment were numbered 56–70, and Patent Owner states that the submitted claims "substantially correspond[] to the allowed claims." Prelim. Resp. 8. We discern no difference (and none has been argued) between submitted claims 56, 66, 67, 69, and 70 and challenged claims 1, 11, 12, 14, and 15, respectively.

including, for example: (1) the similarities and material differences between the asserted art and the prior art involved during examination; (2) the cumulative nature of the asserted art and the prior art evaluated during examination; (3) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection; (4) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art; (5) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and (6) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments. *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, Case IPR2017-01586, slip op. at 17–18 (PTAB Dec. 15, 2017) (Paper 8) (informative). After considering these factors, we are persuaded that the Petition presents the same or substantially the same prior art or arguments that previously were presented to the Office with respect to the asserted ground of anticipation based on the '241 patent as characterized by Patent Owner's Admissions, and exercise our discretion to deny institution on the basis of this anticipation challenge. *See* 35 U.S.C. § 325(d).

Petitioner's Arguments Regarding Section 325(d)

Petitioner states that "[t]here is no basis to deny the instant petition under 35 U.S.C. § 325(d)." Pet. 66. In support of that contention, Petitioner states that:

a. The Petition is the first time the '921 patent has been challenged before the Office since its issuance;[13]

[13] Our analysis under 35 U.S.C § 325(d) is not based on prior petitions or other post-grant challenges to the '921 patent, but Section 325(d) is also applicable to prior art or arguments set forth in the prosecution history. *See Neil Ziegmann*, at slip op. 29–30.

b. The Examiner never cited Bartoszyk in any office action rejection, and did not discuss Bartoszyk in the "Reasons for Allowability;"[14]

c. The Examiner was incorrect in finding that the '241 patent did not teach crystalline forms, because the Examiner failed to consider that the specification of the '241 patent disclosed that the Examples were worked up by "crystallization;"

d. The Examiner did not correctly identify Example 4 of the '241 patent as the closest prior art;

e. The Patent Owner's Admissions state clearly that Example 4 of the '241 patent was a mixture of amorphous and crystalline VHCl;[15] and

f. The '241 patent discloses that Example 4 has a discrete melting point range, which is indicative of crystallization. Pet. 66–67.

Patent Owner's Arguments Regarding Section 325(d)

Patent Owner contends that we should deny institution because "Petitioner's primary art and arguments were already considered by the Examiner during prosecution of the '921 patent." Prelim. Resp. 51. Patent Owner argues that the '241 patent was expressly considered by the Examiner and found not to teach the claimed crystalline forms, and that "the so-called Patent Owner Admissions relied on by Petitioner come from the '921 specification, which was before and considered by the Examiner during prosecution." *Id.* Patent Owner further argues

[14] Petitioner also refers to "Brittain" (Ex. 1010) but Brittain was not cited in the patentability challenges. Prelim. Resp. 52.

[15] The asserted Patent Owner's Admissions actually state that Example 4 was a mixture of crystalline VHCl, amorphous VHCl, and vilazodone free base. *See* discussion at II.C.2. *supra*.

that the Examiner considered other patents having the same specification as the '921 patent, and that Bartoszyk was considered by the Examiner. *Id.*

We address the above factors[16] under Section 325(d) in view of the prosecution history and the parties' arguments.[17]

Factors 1–3

Both the '241 patent and Patent Owner's Admissions were before and considered by the Examiner in connection with claims 1, 14, and 15. *See* Ex. 1001, Ex. 1006, 8, and II.C.2, *supra*.

Factor 5

Petitioner contends that the Examiner erred in evaluating the art asserted in this anticipation challenge because the Examiner incorrectly found that the '241 patent did not teach crystalline forms, purportedly because the Examiner failed to consider that the specification of the '241 patent disclosed that the Examples were worked up by "crystallization" (Petitioner argument c. above). We do not find this to be a sufficient showing of error by the Examiner. First, the Examiner did not find "that the '241 patent did not teach crystalline forms," but that the '241 patent did not "teach the *claimed* crystalline forms." Ex. 1006, 8 (emphasis added). Second, as pointed out by Patent Owner (Prelim. Resp. 14–17), the specification of the '241 patent does not state that the Examples were worked up by crystallization, but that the phrase "'working-up in conventional manner' means: . . . and the residue is purified by *chromatography and/or crystallization*." Ex. 1004, 9:3–8

[16] Factor 4 is inapplicable because no arguments regarding the challenged claims were made during examination.

[17] For purposes of our decision to decline institution, we also note that Petitioner argues that the treatment method of dependent claim 14 and the composition of dependent claim 15 are disclosed by the '241 patent. Pet. 21–23.

(emphasis added). Neither Example 3 nor Example 4 (which references Example 3) of the '241 patent uses the phrase "working-up in conventional manner." *See id.* at 10:57–11:24; Prelim. Resp. 14–17. Nevertheless, this argument is not a sufficient showing that the Examiner erred in evaluating the '241 patent.

Petitioner also contends that the Examiner erred by not identifying Example 4 as the closest prior art, arguing further that Example 4 was a mixture of amorphous and crystalline VHCl (and vilazodone free base), and that "Example 4 has a discrete melting point range, which is indicative of crystallization." Pet. 67 (Petitioner arguments d, e, and f above). We do not find this to be a sufficient showing of error by the Examiner. First, the Examiner identified the '241 patent as the closest prior art, which included Example 4, and we find no persuasive reason for the Examiner to have narrowed "the closest prior art" to a specific example within the '241 patent, particularly where the specification of the '921 patent specifically discusses Example 4.

Second, Petitioner argues that, based on the Patent Owner's Admissions, Example 4 was a mixture of amorphous VHCl, crystalline VHCl, and vilazodone free base, and that its melting point range is indicative of crystallization. Pet. 4–5, 67. However, Petitioner does not sufficiently show that the disclosure of a compound that is such a mixture is an anticipatory disclosure of a compound "which is [VHCl] in its crystalline modification" as claimed.[18] *See* II.B. *supra*.

[18] Petitioner argues that the '241 patent anticipates because it inherently discloses crystalline VHCl. Pet. 19. However, Petitioner's Declarant states that "[a] POSA would recognize that the 269–272 °C melting point was *more likely than not* measured from the crystalline modification of vilazodone hydrochloride." Ex. 1002 ¶ 142 (emphasis added). But, as Petitioner acknowledges, a showing of inherency requires "that [the] missing characteristic is *necessarily present* . . . in the single anticipating reference." Pet. 19 (quoting *SmithKline Beecham Corp. v.*

Additionally, the fact that Example 4 provides a melting point range of 269–272° does not support a sufficient showing of error by the Examiner because, although Dr. Rogers opines that, based on this "narrow melting point range," a person of ordinary skill in the art "would recognize that the majority of the mixture is crystalline VHCl,"[19] Dr. Rogers also acknowledges that "neither the [Patent Owner's Admissions] of the '921 patent nor Example 4 of the '241 patent indicate how much amorphous VHCl or vilazodone free base is present in the mixture." *Id.* ¶ 143.

Therefore, Petitioner does not sufficiently show that the Examiner erred in concluding that the '241 patent did "not teach the claimed crystalline forms" and that challenged claims 1, 14, and 15 "are novel . . . over the prior art." Ex. 1006, 8.

Factor 6

Petitioner has not sufficiently shown that additional evidence or facts warrant reconsideration of the prior art.

Accordingly, pursuant to 35 U.S.C. § 325(d), we exercise our discretion and decline to institute an *inter partes* review on the ground of anticipation of claims 1, 14, and 15 by the '241 patent, as characterized by Patent Owner's Admissions.

D. Obviousness over the '241 patent, as characterized by Patent Owner's Admissions, in view of Bartoszyk

Petitioner contends that claims 1, 14, and 15 are obvious over the '241 patent, as characterized by Patent Owner's Admissions, in view of Bartoszyk. Pet. 23–31. For the reasons set forth below, we exercise our discretion to decline

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Apotex Corp., 493 F.3d 1331, 1343 (Fed. Cir. 2005)) (emphasis added).

[19] Patent Owner disputes this conclusion, and argues that two amorphous forms of vilazodone hydrochloride have been reported to exhibit melting points of 281.54 °C and 278.77 °C, respectively. Prelim. Resp. 17–18, citing Ex. 2015, Figures 47–48; ¶¶ 58–59.

institution because the same or substantially the same prior art or arguments were previously presented to the Office. *See* 35 U.S.C. § 325(d).

1. Bartoszyk (Ex. 1005)

Bartoszyk is directed to vilazodone hydrochloride and its use in treating certain medical disorders. Ex. 1005, Abstract; Ex. 1001, 1:35–41.

2. Analysis

Our analysis regarding the '241 patent and Patent Owner's Admissions, as set forth above, is hereby applied for purposes of this obviousness challenge.

Factors 1–3

Petitioner argues that the Examiner never cited Bartoszyk in any office action rejection, and did not discuss Bartoszyk in the "Reasons for Allowability." Pet. 66. However, Bartoszyk was referenced in the background section of the '921 patent and considered by the Examiner. Ex. 1001, 1:41, pg. 1 (References Cited). Moreover, the disclosure of Bartoszyk relied on by Petitioner is essentially cumulative to the teachings of the '241 patent, and Petitioner does not identify any material differences between Bartoszyk and the '241 patent. *Id*. at 1:35–41; Pet. 26. For at least these reasons, the fact that the Examiner never cited Bartoszyk "in any office action rejection" and did not discuss Bartoszyk in the "Reasons for Allowability," does not sufficiently show that the same (or substantially the same) art as now asserted was not before and considered by the Examiner.

Factor 5

Petitioner does not sufficiently show that the Examiner erred in evaluating the prior art and concluding that the challenged claims "are . . . non-obvious over the prior art." Ex. 1006, 8. For example, Petitioner does not sufficiently addresses (if at all) the Examiner's finding that "[a] person of ordinary skill in the art would not have expected that making modifications would retain identical activity as

disclosed in the prior art." *Id.* Rather, Petitioner simply recasts the same information that was before and considered by the Examiner in the form of an obviousness challenge rather than sufficiently showing how the Examiner erred in applying that information. Pet. 23–31. Moreover, Patent Owner persuasively argues both the insufficiency of "a general motivation to obtain crystalline forms" and the unpredictability of crystalline forms. *See* Prelim. Resp. 29–34.

Factor 6

Petitioner has not sufficiently shown that additional evidence or facts warrant reconsideration of the prior art.

Accordingly, pursuant to 35 U.S.C. § 325(d), we exercise our discretion and decline to institute *inter partes* review of claims 1, 14, and 15 on the ground of obviousness over the '241 patent, as characterized by Patent Owner's Admissions, in view of Bartoszyk.

E. Obviousness over the '241 patent, as characterized by Patent Owner's Admissions, in view of Pavia and Byrn

Petitioner contends that claims 1 and 11 are obvious over the '241 patent, as characterized by Patent Owner's Admissions, in view of Pavia and Byrn. Pet. 31–50. For the reasons set forth below, we exercise our discretion to decline institution because the same or substantially the same prior art or arguments were previously presented to the Office. *See* 35 U.S.C. § 325(d).

1. Pavia (Ex. 1032) and Byrn (Ex. 1012)

Pavia and Byrn are excerpts from textbooks that purport to show routine crystallization techniques and analysis of crystalline solids that would have been known to a person of ordinary skill in the art at the time of the invention. Pet. 14–15; 33–35, 50; Ex. 1002 ¶¶ 106–111, 136, 137. Patent Owner argues that neither

Pavia nor Bryn "teach or suggest vilazodone hydrochloride, let alone its crystalline forms." Prelim. Resp. 51–52.

2. Analysis

Our analysis regarding the '241 patent and Patent Owner's Admissions, as set forth above, is hereby applied for purposes of this obviousness challenge.

Pavia and Byrn were not considered by the Examiner during prosecution of the '921 patent. In addressing Section 325(d), Petitioner relies on its arguments regarding the '241 patent and Patent Owner's Admissions. Pet. 66–67.

Factors 1–3

Both the '241 patent and Patent Owner's Admissions were before and considered by the Examiner in connection with claims 1 and 11. *See* Ex. 1001, Ex. 1006, 8, and II.C.2, *supra*. Although Pavia and Byrn were not considered by the Examiner, Petitioner cites both the '241 patent and Pavia for the contention that "[v]arious routine techniques to purify pharmaceutically active compounds were well known, including crystallization." Pet. 17. In connection with this obviousness challenge, Petitioner also relies on Byrn for teaching crystallization techniques, such as comparison of X-ray powder diffraction data. *Id.* at 34–35; 44–45. Accordingly, based on Petitioner's arguments, we find that that Pavia or Byrn are substantially cumulative to the '241 patent with respect to crystallization techniques for which they are cited. Moreover, given that Pavia and Byrn appear to be introductory textbooks, Petitioner does not sufficiently show that the Examiner would not have been aware of such crystallization techniques relied upon by Petitioner. *See* Ex. 1032, Title; Ex. 1012, 4 ("It is hoped that the reader

will gain an appreciation of what this discipline encompasses by reading this chapter.").

Factor 5

As discussed above, Petitioner has not sufficiently shown how the Examiner erred in evaluating the prior art.

Factor 6

This factor considers the extent to which the additional evidence and facts warrant reconsideration of the art that was before and considered by the Examiner. For the reasons set forth below, we find that Petitioner's analysis, based on Pavia and Byrn, does not warrant reconsideration of the art considered by the Examiner.

Petitioner's obvious challenge to claims 1 and 11 relies on experiments (referred to as the Second and Fifth Experiments) carried out by Dr. Gurau under the direction and supervision of Dr. Rogers. Ex. 1002 ¶ 182. The purpose of those experiments was to "determine whether vilazodone hydrochloride in its crystalline modification ('Form IV') [claim 11] is obtained using routine recrystallization techniques that a POSA would have known and performed on the prior art Example 4 mixture disclosed in the '241 patent." *Id.* ¶ 183. According to Petitioner, the results of those experiments show that "a POSA purifying Form VIII, as in Example 4 of the '241 patent, via recrystallization to remove any amorphous or free base vilazodone would have obtained Form IV, as recited in claim 11 of the '921 patent." Pet. 43. In conducting those experiments, Drs. Rogers and Gurau apparently relied on techniques shown in Pavia and Byrn. Pet. 37–45.

The subject experiments used commercial vilazodone hydrochloride, purchased from Boc Sciences, as the starting material. Ex. 1002 ¶ 184. That purchased product was determined to be "pure, crystalline vilazodone

hydrochloride in Form VIII." *Id.* ¶ 185. In the opinion of Dr. Rogers, the use of the purchased pure Form VIII rather than the vilazodone hydrochloride mixture set forth in Example 4 of the '241 patent or the Patent Owner's Admissions would "not likely result in different recrystallization outcomes." *Id.* ¶ 190.

We find that the additional evidence and facts do not warrant a reconsideration of the Examiner's conclusion. As an initial matter, both Dr. Rogers and Dr. Gurau have a level of skill well beyond that of a person of ordinary skill in the art, thereby weakening any argument that successful experiments by Drs. Rogers and Gurau evidence a reasonable expectation of success by a person of ordinary skill in the art. *Compare* Exs. 1023 and 1039 *with* II.A. *supra*. Moreover, the subject experiments began with the objective of determining whether *claimed* Form IV could be obtained, beginning with Form VIII. Ex. 1002 ¶ 185. In our view, and as Patent Owner argues (Prelim. Resp. 40–47), such an approach by Petitioner involves improper hindsight. Here, a backward looking effort to create the claimed Form IV from purchased Form VIII, more than sixteen years after the effective filing date of the '921 patent,[20] cannot form the basis for an obviousness determination. *See* 35 U.S.C. § 103(a). Furthermore, the fact that Petitioner's experiments and cited textbooks (Pavia and Bryn) were not before the Examiner does not warrant reconsideration of the art that was before and considered by the Examiner, at least because of this fundamentally flawed analysis by Petitioner.

None of Petitioner's obviousness arguments that rely on Pavia and Bryn (or Petitioner's experiments) show sufficiently that the Examiner's conclusion of

[20] Dr. Gurau indicates that the experiments were performed between October 23, 2017, and December 12, 2017. Ex. 1039, 2.

nonobviousness should be reconsidered. Those arguments include, for example, the "obvious to try" argument wherein Petitioner refers to the Second and Fifth Experiments as showing that "a POSA would have a reasonable expectation of success." Pet. 47.

Accordingly, pursuant to 35 U.S.C. § 325(d), we exercise our discretion and decline to institute *inter partes* review of claims 1 and 11 on the ground of obviousness over the '241 patent, as characterized by Patent Owner's Admissions, in view of Pavia and Byrn.

F. Obviousness over the '241 patent, as characterized by Patent Owner's Admissions, in view of Bartoszyk, Pavia, and Byrn

Petitioner contends that claims 1, 12, 14, and 15 are obvious over the '241 patent, as characterized by Patent Owner's Admissions, in view of Bartoszyk, Pavia, and Byrn. Pet. 50–62. For the reasons set forth below, we exercise our discretion to decline institution because the same or substantially the same prior art or arguments were previously presented to the Office. *See* 35 U.S.C. § 325(d).

1. Analysis

Our analysis regarding the '241 patent, as characterized Patent Owner's Admissions, Bartoszyk, Pavia, and Byrn, as set forth above, is hereby applied for purposes of this obviousness challenge. As to claims 1, 14, and 15, Petitioner essentially restates its arguments as advanced in connection with Grounds 1, 2, and 3. Pet. 54–62. For the reasons set forth above, we exercise our discretion to decline institution of *inter partes* review with respect to claims 1, 14, and 15.

Claim 12 is not the subject of any other challenge advanced by Petitioner. Claim 12 generally recites a method of treating a patient by administering the pharmaceutical composition of claim 11. Ex. 1001, 28:10–20. Claim 12 recites the same disorders as recited in method claim 14, but recites administering the

composition of claim 11 rather than the compound of claim 1. *Compare* Ex. 1001, 28:10–20 *with* Ex. 1001, 28:34–44. Accordingly, for the reasons set forth above regarding claims 11 and 14, we decline to institute *inter partes* review as to claim 12.

Accordingly, pursuant to 35 U.S.C. § 325(d), we exercise our discretion and decline to institute *inter partes* review of claims 1, 12, 14, and 15 on the ground of obviousness over the '241 patent, as characterized by Patent Owner's Admissions, in view of Bartoszyk, Pavia and Byrn.

III. CONCLUSION

The '241 patent, the background section of the '921 patent, and Bartoszyk were all before and considered by the Examiner. Moreover, Petitioner has not shown sufficiently how the Examiner erred in determining that the challenged claims were "novel and nonobvious over the prior art." Ex. 1006, 8. Neither the citation of textbooks (Pavia and Byrn) regarding crystallization techniques and analysis, nor Petitioner's arguments and declaratory evidence, provide sufficient additional evidence or facts to justify reconsideration of the Examiner's decision. Additionally, in balancing the appropriate factors, we are not persuaded that adjudicating a dispute over the same base reference that was considered and discussed by the Examiner is an efficient use of Board or party resources. Accordingly, we exercise our discretion under 35 U.S.C. § 325(d) and do not institute *inter partes* review of the challenged claims.

IV. ORDER

In consideration of the foregoing, it is hereby ORDERED that the Petition is *denied*.

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