IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTELLAS PHARMA INC., *et al.*,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	Civil Action No. 16-905-JFB-CJB
	)	Consolidated
ACTAVIS ELIZABETH LLC, *et al.*,	)	
	)	
Defendants.	)	

REPORT AND RECOMMENDATION

In these consolidated Hatch-Waxman actions filed by Plaintiffs Astellas Pharma Inc., Astellas Ireland Co., Ltd. ("AICL") and Astellas Pharma Global Development, Inc. ("APGD" and collectively with other Plaintiffs, "Astellas" or "Plaintiffs") against Actavis Elizabeth LLC, Lupin Ltd. and Lupin Pharmaceuticals, Inc., Zydus Pharmaceuticals (USA), Inc. and Cadila Healthcare Ltd., Aurobindo Pharma Ltd., Aurobindo Pharma USA, Inc. and Aurolife Pharma LLC (collectively, "Aurobindo"), Prinston Pharmaceutical Inc., Sandoz Inc., Sawai Pharmaceutical Co., Ltd. and Sawai USA, Inc. (collectively, "Sawai" and together with Aurobindo, "SA Defendants"), and Apotex Inc. and Apotex Corp., Plaintiffs allege infringement by all Defendants ("Defendants") of, *inter alia*, U.S. Patent Nos. 7,342,117 (the "'117 patent") and 7,982,049 (the "'049 patent"). Presently before the Court is the matter of claim construction. The Court recommends that the District Court adopt the constructions as set forth below.

I. BACKGROUND

A. The Parties

Astellas Pharma Inc. is the record owner and assignee of the '117 patent and the '049 patent, and AICL is the exclusive licensee of the patents. (D.I. 1 at ¶¶ 42-43) APGD has contracted with Astellas Pharma US, Inc., a subsidiary of Astellas Pharma Inc., to market and sell the drug mirabegron under the trade name Myrbetriq®. (*Id.* at ¶¶ 39, 44) Myrbetriq tablets

are indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency. (*Id.* at ¶ 41)

Defendants are in the business of developing, manufacturing and distributing generic versions of branded drug products throughout the United States. (*See, e.g.*, *id.* at ¶ 4)

B. The '117 and '049 Patents[1]

The '117 patent and the '049 patent are both entitled "α-Form or β-Form Crystal of Acetanilide Derivative." (D.I. 1, exs. B, C (hereinafter, the "'117 patent" and the "'049 patent")) The '049 patent is a continuation of the U.S. patent application that led to the '117 patent, and the patents therefore share a specification. (*See* '049 patent; D.I. 77 at 2) Both patents claim priority to PTC Application No. PCT/JP02/11217, filed on October 29, 2002, and to Japanese Patent No. JP2001-332914, filed on October 30, 2001. ('117 patent; '049 patent; D.I. 77 at 2) The '117 patent issued on March 11, 2008, ('117 patent), and the '049 patent issued on July 19, 2011, ('049 patent). The '117 patent claims crystal forms of mirabegron, and the '049 patent claims pharmaceutical compositions comprising crystal forms of mirabegron and a pharmaceutically acceptable carrier, as well as methods of treating diabetes utilizing the claimed pharmaceutical compositions. ('117 patent, col. 12:18-30; '049 patent, cols. 11:5-12:33; D.I. 1 at ¶¶ 27, 30)

C. Technical Overview

Solids can exist in crystalline form, meaning the atoms (or molecules) are arranged in a

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[1] Plaintiffs also allege infringement of United States Patent Nos. 6,346,532, 8,835,474 and RE44,872, but the parties have not identified any claim construction issues involving those patents. (*See, e.g.*, D.I. 1 at ¶ 10; D.I. 73 at 1)

repeating and ordered pattern that extends in three dimensions to form the crystal. (D.I. 78 at ¶ 29; D.I. 97 at ¶ 25)[2] Many compounds have the ability to crystallize into more than one distinct crystal form, with the atoms packed differently in the crystal's structure from form to form; these different crystalline forms of the same substance are referred to as polymorphs. (D.I. 78 at ¶ 30; D.I. 97 at ¶ 26) For example, the molecules of an active pharmaceutical ingredient ("API") may exist in more than one crystalline form. (D.I. 78 at ¶ 30) Polymorphs of an API may have differing properties, such as solubility, hygroscopicity,[3] dissolution rate and chemical and thermal stability. (*Id.*) Each new crystal form is generally given a formal name using sequential Roman numerals, Arabic numerals, or Greek or Latin letters. (*Id.* at ¶ 39; D.I. 97 at ¶ 28) Each "Form X" name for a different polymorph refers to a unique, specific crystalline form having its own characteristics. (D.I. 78 at ¶¶ 30, 39; D.I. 97 at ¶ 28)

Powder x-ray diffraction (known as "XRPD") is a common method that has been used for many years in the pharmaceutical industry to help characterize and distinguish different crystalline forms. (D.I. 78 at ¶ 31; D.I. 97 at ¶ 30) This method tests a small amount of crystalline powder (instead of a single crystal) by exposing the sample to x-rays. (D.I. 78 at ¶ 31) X-ray diffraction results when x-rays of particular wavelengths are directed at a sample; the diffraction angles are measured, and an observable pattern of peaks is created that serves as a

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[2] Solids can also exist in amorphous form, meaning their molecules are similarly oriented for no more than a few molecules—unlike crystalline forms, they have no "long-range" order. (D.I. 78 at ¶ 29)

[3] Hygroscopicity refers to the propensity of a particular crystal form to absorb moisture from the air. (D.I. 78 at ¶¶ 45, 80)

fingerprint for each unique crystal structure. (*Id.* at ¶¶ 31-32; D.I. 97 at ¶¶ 30-31, 35) These patterns of peaks can be placed on a chart, known as an "x-ray diffraction diagram" or "x-ray diffractogram," so that all of these peaks (including those peaks that stand out as being the most intense) can be viewed at one time. (*See, e.g.*, '049 patent at FIGS. 1, 3-4; D.I. 97 at ¶ 32)

Another well-established analytical technique that can be used to characterize crystal forms is differential scanning calorimetry ("DSC"). (D.I. 78 at ¶ 40; D.I. 97 at ¶ 40) One property of a polymorph is its melting point and associated endotherm, which measures the temperature at which the compound turns from solid to liquid as well as the heat absorbed during the process. (D.I. 97 at ¶ 40) DSC measures the melting point of a sample by analyzing the difference in the amount of heat flowing between two pans sitting on top of two separate heaters—a sample pan and a reference pan left empty. (D.I. 78 at ¶ 41; D.I. 97 at ¶ 40) When a sample melts, energy is required, and this event is reflected by a peak in the DSC profile representing the energy required to melt the crystal. (D.I. 78 at ¶ 42; D.I. 97 at ¶ 40)

D. Procedural History

This litigation arises from each of Defendants' submissions of Abbreviated New Drug Applications ("ANDAs") to the United States Food and Drug Administration ("FDA"), which seek approval to market generic versions of Myrbetriq. (*See, e.g.*, D.I. 1 at ¶ 45; D.I. 77 at 1) APGD is the holder of New Drug Application No. 202611, which covers Myrbetriq. (D.I. 1 at ¶ 39) Plaintiffs filed the instant cases in October 2016, alleging, *inter alia*, that Defendants' ANDA products and the use thereof would infringe at least claim 1 of the '117 patent and certain claims of the '049 patent pursuant to 35 U.S.C. § 271(a), and that Defendants' submission of

their ANDAs constituted acts of infringement of certain claims of the '049 patent pursuant to 35 U.S.C. § 271(e)(2). (*See, e.g.*, D.I. 1 at ¶¶ 57, 60-61)[4]

On August 10, 2017, Judge Joseph F. Bataillon referred "all dispositive and nondispositive matters on all issues, including claim construction, except for summary judgments, Daubert motions and pretrial motions in limine[]" to the Court. (D.I. 67) The parties completed lengthy briefing on claim construction on March 21, 2018. (D.I. 77, 93, 95, 112, 146, 148, 155, 156) The Court held a *Markman* hearing on March 23, 2018. (D.I. 163 (hereinafter, "Tr.")) The Scheduling Order states that the Court "shall issue its decision on claim construction on or before June 20, 2018." (D.I. 25 at 9 (emphasis omitted))

II. STANDARD OF REVIEW[5]

A. Claim Construction

It is well-understood that "[a] claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using, or selling the protected invention." *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989). Claim construction is a generally a question of law, although subsidiary fact finding is sometimes necessary. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837-38 (2015).

The Court should typically assign claim terms their "'ordinary and customary meaning[,]'" which is "the meaning that the term[s] would have to a person of ordinary skill in

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[4] The cases have been consolidated for all purposes. (D.I. 25 at 4)

[5] Because Defendants contend that each of the disputed claim terms are indefinite, (*see, e.g.*, D.I. 93 at 20), the Court includes herein the applicable standards for both claim construction and definiteness.

the art ['POSA'] in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (citations omitted). However, when determining the ordinary meaning of claim terms, the Court should not extract and isolate those terms from the context of the patent, but rather should endeavor to reflect their "meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321; *see also Eon Corp. IP Holdings LLC v. Silver Spring Networks, Inc.*, 815 F.3d 1314, 1320 (Fed. Cir. 2016).

In proceeding with claim construction, the Court should look first and foremost to the language of the claims themselves, because "[i]t is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips*, 415 F.3d at 1312 (internal quotation marks and citations omitted). For example, the context in which a term is used in a claim may be "highly instructive." *Id.* at 1314. In addition, "[o]ther claims of the patent in question, both asserted and unasserted, can . . . be valuable" in discerning the meaning of a particular claim term. *Id.* This is "[b]ecause claim terms are normally used consistently throughout the patent, [and so] the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Id.* Moreover, "[d]ifferences among claims can also be a useful guide[,]" as when "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15.

In addition to the words of the claims, the Court should look to other intrinsic evidence. For example, the Court should analyze the patent specification, which "may reveal a special definition given to a claim term . . . that differs from the meaning [that term] would otherwise

possess" or may reveal an intentional disclaimer of claim scope. *Id.* at 1316. Even if the specification does not contain such revelations, it "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Id.* at 1315 (internal quotation marks and citation omitted). That said, however, the specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004). And a court should also consider the patent's prosecution history, if it is in evidence, because it "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution[.]" *Phillips*, 415 F.3d at 1317.

Extrinsic evidence, "including expert and inventor testimony, dictionaries, and learned treatises[,]" can also "shed useful light on the relevant art[.]" *Id.* (internal quotation marks and citations omitted). Overall, while extrinsic evidence may be useful, it is "less significant than the intrinsic record in determining the legally operative meaning of claim language." *Id.* (internal quotation marks and citations omitted); *accord Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 981 (Fed. Cir. 1995).

In utilizing these resources during claim construction, courts should keep in mind that "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998).

B. Definiteness

35 U.S.C. § 112 ("Section 112") requires that a patent claim "particularly point[] out and distinctly claim[] the subject matter which the applicant regards as his invention." 35 U.S.C. §

112, ¶ 2.[6] If it does not, the claim is indefinite and therefore invalid. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2125 (2014) ("*Nautilus*"). In *Nautilus*, the Supreme Court of the United States set out the test to be applied in the definiteness inquiry: "a patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Id.* at 2124. Definiteness is to be evaluated from the perspective of a POSA at the time the patent was filed. *Id.* at 2128.

Like claim construction, definiteness is a question of law for the court. *H-W Tech., L.C. v. Overstock.com, Inc.*, 758 F.3d 1329, 1332 (Fed. Cir. 2014); *Pi-Net Int'l Inc. v. JPMorgan Chase & Co.*, 42 F. Supp. 3d 579, 586 (D. Del. 2014). The United States Court of Appeals for the Federal Circuit has stated that "[a]ny fact critical to a holding on indefiniteness . . . must be proven by the challenger by clear and convincing evidence." *Intel Corp. v. VIA Techs., Inc.*, 319 F.3d 1357, 1366 (Fed. Cir. 2003); *see also Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1338 (Fed. Cir. 2008).[7]

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[6] Here, the Court refers to the text of Section 112 as it read prior to the passage of the Leahy-Smith America Invents Act, since the patent applications leading to the patents at issue here were filed well before September 16, 2012. ('117 patent; '049 patent); *see also Q.I. Press Controls, B.V. v. Lee*, 752 F.3d 1371, 1374 n.2 (Fed. Cir. 2014).

[7] In *Nautilus*, the Supreme Court left open the question of whether factual findings subsidiary to the ultimate issue of definiteness should, in fact, trigger the application of a "clear-and-convincing-evidence standard[,]" noting that it would "leave th[is] question[] for another day." *Nautilus*, 134 S. Ct. at 2130 n.10. In the absence of Supreme Court precedent to the contrary, the Federal Circuit's case law (utilizing the clear-and-convincing-evidence standard) controls. *See Cal. Inst. of Tech. v. Hughes Commc'ns Inc.*, 35 F. Supp. 3d 1176, 1182 n.4 (C.D. Cal. 2014).

The primary purpose of the definiteness requirement is to ensure that patent claims are written in such a way that they give notice to the public of what is claimed, thus enabling interested members of the public (e.g., competitors of the patent owner) to determine whether they infringe. *All Dental Prodx, LLC v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779-80 (Fed. Cir. 2002). Put another way, "[a] patent holder should know what he owns, and the public should know what he does not." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722, 731 (2002). Even so, the Supreme Court has recognized that "absolute precision is unattainable" and not required. *Nautilus*, 134 S. Ct. at 2129.

III. DISCUSSION

The Court takes up the three sets of disputed terms in the order in which the parties addressed them at the *Markman* hearing.[8]

A. "α-form crystal" and "β-form crystal"

The claim term "α-form crystal" appears in claim 1 of the '049 patent, and the claim term "β-form crystal" appears in claim 3 of that patent. Claims 1 and 3 are reproduced below:

> **1.** A solid pharmaceutical composition comprising the *α-form crystal* of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide and a pharmaceutically acceptable carrier.

('049 patent, col. 11:5-8 (emphasis added))

> **3.** A solid pharmaceutical composition comprising the *β-form crystal* of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide and a pharmaceutically acceptable carrier.

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[8] The parties originally submitted a fourth term for claim construction: "at around," found in claims 1 and 2 of the '117 patent. (*See* D.I. 73, ex. A) Prior to claim construction briefing, however, the parties agreed to construe the term to mean "± 0.20 °2Θ." (D.I. 77 at 1 n.2)

(*Id.*, col. 11:14-17 (emphasis added))

Plaintiffs explain that the terms "α-form crystal" and "β-form crystal" are "the names of the two novel crystal forms of mirabegron that are described in the specification" of the '049 patent. (D.I. 77 at 10) Defendants agree on this point, characterizing the terms as "arbitrary identifiers given to polymorphs of a given compound." (D.I. 93 at 12) With respect to the proper constructions of these claim terms, Plaintiffs propose that "α-form crystal" be construed to mean "α-form crystal which is a term of reference for a polymorphic crystal form of (R) 2-(2-aminothiazol-4-yl)-4'-[2-[(2 hydroxy-2-phenylethyl)amino]ethyl]acetanilide that can be distinguished from other forms." (D.I. 77 at 10) Likewise, as to "β-form crystal," Plaintiffs propose that the term be construed to mean "β-form crystal which is a term of reference for a polymorphic crystal form of (R) 2-(2-aminothiazol-4-yl)-4'-[2-[(2 hydroxy-2-phenylethyl)amino]ethyl]acetanilide that can be distinguished from other forms." (*Id.*)

For their part, Defendants assert that the terms are indefinite. (D.I. 93 at 12) Defendants contend that since these terms do not have ordinary or customary meanings, the specification of the '049 patent must provide sufficient data that would allow the POSA to actually identify each form. (*Id.* at 12-13) According to Defendants, the specification fails to do so. (*Id.*) Instead, Defendants contend that the "minimal descriptions" of each form of crystal in the specification "are often inconsistent and contradictory" and thus cannot be used to determine whether a sample falls within the scope of the α-form or β-form crystal. (*Id.*at 13; *see also* D.I. 146 at 4; Defendants' Claim Construction Arguments Presentation, Slides A9-A10) As for Plaintiffs' proposed constructions, Defendants point out that Plaintiffs' proposals fail to actually identify any further characteristics of the α-form and β-form crystals, and therefore just "[c]onfirm [that] the [t]erms [a]re [i]ndefinite[.]" (D.I. 93 at 15; Tr. at 30 (Defendants' counsel explaining that

Plaintiffs' proposed construction for "α-form crystal[,]" for example, essentially states that the "alpha form means alpha form"))

Below, the Court addresses the key issues raised by the parties' respective positions.

1. Why Plaintiffs' Proposed Constructions Are Not Acceptable

The Court finds that Plaintiffs' proposed constructions for the terms "α-form crystal" and "β-form crystal" are problematic. This is because, as Defendants point out, the constructions do not provide any further clarification as to how the two terms can be distinguished from each other. (D.I. 93 at 15)[9]

Plaintiffs argue that their proposed constructions are sufficient because: (1) once a new crystalline form has been identified and described, it will have a "chemical structure and a host of physical characteristics that can be used to identify it"; but (2) a POSA would find it unnecessary to recite all of these characteristics in order to identify the forms, since the POSA could make that identification simply by hearing the name for the form. (D.I. 77 at 13; Tr. at 61 (Plaintiffs' counsel contending that, if the claims used the word "mirabegron," for instance, that is just a name, but the name "tells you exactly what the thing is, because from the patent or from

[9] Another problem with Plaintiffs' proposed constructions is that their breadth would permit the α-form and β-form crystals to be defined by methods not disclosed in the specification. (*See* D.I. 93 at 15-16; D.I. 97 at ¶ 77) To that end, Plaintiffs assert that a POSA would be aware of additional methodologies not discussed in the specification (but commonly used by POSAs) that could be used to identify, characterize and distinguish the α-form crystal and β-form crystal, such as: IR spectroscopy, Raman spectroscopy, solid state NMR and single crystal x-ray diffraction. (D.I. 77 at 14; D.I. 112 at 4; D.I. 78 at ¶ 74; *see also* Tr. at 43) However, Plaintiffs (and their expert) provided no further explanation as to "how these methods may be used and their data evaluated to distinguish the α-form and β-form crystals from other solid forms of mirabegron and each other." (D.I. 93 at 16 (citing D.I. 97 at ¶ 77); *see* D.I. 78 at ¶ 74) Thus, the Court is not persuaded that the constructions for these terms should allow for the use of additional methodologies in order to determine whether one of the forms is present.

other sources, there's lots of identifying information that tells you what mirabegron is")) The problem with Plaintiff's position, however, is that we have a fundamental *dispute* here about the terms—i.e., whether there is sufficient guidance in the intrinsic record to allow the POSA to distinguish the α-form crystal and β-form crystal from each other (and if so, what is that guidance)? Were the Court to simply adopt Plaintiffs' proposed constructions, this would not resolve the dispute.[10] *See, e.g.*, *Celgene Corp. v. Natco Pharma Ltd.*, Civil Action No. 10-5197 (SDW), 2014 WL 2196941, at *4 (D.N.J. May 27, 2014) (rejecting plaintiff's proposal to construe "Form A" to mean "a polymorphic form of 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)piperidine-2,6-dione that can be distinguished from other forms" because such a construction would "give no meaning to the term 'Form A'" and would "ignore the specific attributes of Form A as defined in the specification"). If the intrinsic record does in fact provide such guidance, then the constructions for these terms should at least make reference to that guidance. If the record provides no such guidance, that would indicate that the terms are indefinite.[11]

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[10] Plaintiffs assert that the use of "form" terms such as "α-form crystal" and "β-form crystal" to identify and distinguish crystal forms from each other is common practice. In support of this proposition, they cite to *Bristol-Myers Squibb Co. v. Mylan Pharms. Inc.*, Civil Action No. 09-651-LPS, 2012 WL 1753670, at *6-7 (D. Del. May 16, 2012) and *Pfizer Inc. v. Dr. Reddy's Labs. Ltd.*, No. Civ. No. 09-943-LPS, 2011 WL 767849, at *4, *6 (D. Del. Feb. 28, 2011). (D.I. 77 at 13-14) It is worth noting, however, that in both of these cases (unlike here), the claims directed to novel crystalline forms included additional information about the characteristic(s) that distinguished the claimed crystal from other forms. (*See* D.I. 93 at 15 n.4) In *Bristol-Myers Squibb Co.*, while the court construed various "form" terms to mean "a polymorphic crystal form of [a substance] that can be distinguished from other forms[,]" the relevant claims recited "different numerical designation[s] corresponding to various XRPD and/or DSC values" that served to distinguish those various polymorphs from one another. 2012 WL 1753670, at *3-7. Likewise, in *Pfizer Inc.*, the Court agreed that the "form" terms were terms of convenience or reference, but in a case where the claims at issue specified particular x-ray diffraction peaks that were displayed by the respective crystal forms. 2011 WL 767849, at *4.

[11] Plaintiffs' counsel suggested during oral argument that this issue of "how

2. Is There Sufficient Evidence in the Intrinsic Record that Can Be Used to Distinguish These Two Crystal Forms from Each Other, so as to Avoid Indefiniteness Concerns (and if so, What Is It)?

Having concluded that Plaintiffs' proposed constructions will not be helpful here, the Court next examines whether the intrinsic record contains sufficient evidence that can be used to teach a POSA, with reasonable certainty, how to distinguish these two different crystal forms from each other?[12] In Plaintiffs' view, "the common specification of the [asserted patents] discloses to a POSA how to identify and distinguish the α-form and β-form crystals of mirabegron." (D.I. 112 at 3; *see also* D.I. 155 at 9 (explaining that Plaintiffs "do not argue that the term 'α-form crystal' or 'β-form crystal' have a meaning independent of and apart from the '117 and '049 Patent specifications"))

The '049 patent's specification does expressly discuss observed properties of the α-form crystal and β-form crystal. Plaintiffs point to the following supporting data described in the specification of the '049 patent for each crystal form:

(1) exemplar XRPD spectrums for each form;

(2) disclosures of the heat absorption peaks for each form revealed by DSC analyses performed under specified conditions;

(3) exemplar DSC thermal analysis for each form showing the heat absorption peaks; and

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do I know [that a crystalline sample]" is covered by the claims is an issue of infringement and not claim construction. (Tr. at 37-39) But how could the factfinder determine "whether the [claim term] reads on the accused product" if there is a dispute between the parties regarding whether and how the α-form crystal or β-form crystal may be sufficiently identified? *Clare v. Chrysler Grp. LLC*, 819 F.3d 1323, 1326 (Fed. Cir. 2016); *see, e.g.*, (D.I. 146, ex. J at 22 (Dr. Myerson acknowledging that in order to understand whether there is infringement of claim 1 of the '049 patent, you "have to . . . understand what the [α-form] crystal is")).

[12] The parties' experts agree that different polymorphs of an API will have unique, important properties. (D.I. 78 at ¶¶ 30, 39; D.I. 97 at ¶ 28)

(4) moisture content analyses demonstrating the respective maximum moisture amount each form is capable of holding.

(D.I. 77 at 12; *see also* D.I. 112 at 3)

More specifically, the specification explains that the patentees discovered the claimed novel α-form and β-form crystals, "[b]oth of [which] are of a free base and are distinguished from each other by powder X-ray diffraction spectrum and DSC analysis." ('049 patent, col. 1:56-66) The patent then goes on to explain that the α-form crystal has a moisture-holding amount of not more than 0.2% over the entire range of relative humidity from 5% to 95%, whereas the β-form crystal holds moisture of about 3%. (*Id.*, col. 2:4-10) Next, the specification notes that "[e]ach of the α-form crystal and the β-form crystal is characterized by the following crystal lattice spacings [2θ(°)] of powder X-ray diffraction spectrum and heat absorption peak of DSC analysis." (*Id.* at 2:16-19) The patent then provides two Tables, one for each form of crystal. (*Id.*, col. 2:29-50) Table 1, which relates to the "α-form [c]rystal[,]" references 8 characteristic XRPD peaks (5.32, 8.08, 15.28, 17.88, 19.04, 20.20, 23.16 and 24.34) of that crystal form. (*Id.*, col. 2:29-40) Table 2, which relates to the "β-form [c]rystal[,]" references 5 characteristic XRPD peaks (9.68, 19.76, 20.72, 22.10 and 23.52) for that crystal form. (*Id.*, col. 2:42-52) These Tables are depicted as follows:

TABLE 1

(α-Form Crystal)

Crystal lattice spacing	Relative intensity
5.32	Strong
8.08	Strong
15.28	Slightly strong
17.88	Slightly strong
19.04	Slightly strong
20.20	Slightly strong
23.16	Slightly strong
24.34	Slightly strong

TABLE 2

(β-Form Crystal)

Crystal lattice spacing	Relative intensity
9.68	Medium
19.76	Slightly strong
20.72	Medium
22.10	Medium
23.52	Medium

(*Id.*, col. 2:29-50) With respect to DSC analysis, the specification then explains that "the α-form crystal had a heat absorption peak at 142 to 146° C., and the β-form crystal had heat absorption peaks at 90 to 110° C. and at 142 to 146° C., respectively." (*Id.*, col. 2:53-56)

In the Court's view, this intrinsic evidence relating to exemplar XRPD spectrums and DSC heat absorption peaks *is* evidence that will allow a POSA to sufficiently distinguish the two relevant crystal forms.[13] Defendants' responsive argument to the contrary seems to be that the

[13] As was previously noted above, the specification also discloses the amount of moisture that each form of crystal can hold. ('049 patent, col. 2:4-12) However, for a few different reasons, the Court does not find it appropriate to make reference to these measurements in its recommended constructions for "α-form crystal" and "β-form crystal." For one, the specification expressly states that the crystal forms "are distinguished from each other by powder X-ray diffraction spectrum and DSC analysis[;]" while the specification goes on to provide the moisture-content capabilities of each crystal, it pointedly did not include such characteristics in the sentence that discusses how to "*distinguish*[the forms] from each other[.]" (*Id.*, col. 1:64-66 (emphasis added); *see also id.*, col. 2:16-19 ("Each of the α-form crystal and the β-form crystal *is characterized by* the following crystal lattice spacings . . . of powder X-ray diffraction spectrum and heat absorption peak of DSC analysis.") (emphasis added)) Second, the XRPD diffractograms and DSC curves are the factors that Plaintiffs emphasized most in their briefing,

intrinsic record fails to teach whether using any one of the disclosures would in fact "be sufficient to distinguish the α- and β-forms from any other crystalline forms, including from each other." (D.I. 93 at 13; *see also* D.I. 146 at 4) The Court does not find this argument persuasive, for the following reasons.

With regard to Defendants' criticism that the record does not allow a POSA to distinguish between the claimed crystalline forms and *any other* crystalline forms, Plaintiffs responded by stating that the α-form crystal and the β-form crystal are the *only* known crystalline polymorphs of mirabegron. (D.I. 155 at 7-8; D.I. 146, ex. J at 12-13, 46; Tr. at 40-41) In their briefing, Defendants retorted that even if this were so, the terms would still be indefinite because, *inter alia*, the specification does not allow the POSA to distinguish either the α-form and β-form crystals from "unknown or undiscovered polymorphs[.]" (D.I. 146 at 4) This would not make the claims indefinite, however. As Plaintiffs explain, for the purpose of definiteness, it is not necessary for a claim to distinguish the invention from products that do not exist and are not yet known. (D.I. 155 at 7-8; Tr. at 41) The Supreme Court has explained that, pursuant to the first Patent Act enacted by Congress in 1790, patentees were required to "file a written specification

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when describing what best "characterize[s], identif[ies], and distinguish[es]" the two crystalline forms. (D.I. 112 at 3-4) And third, the Court notes that dependent claims 9 and 11 depend from claims 1 and 3 and that they simply add that "the α-form crystal . . . contains less than 0.2% of moisture" and "the β-form crystal . . . contains less than 3% of moisture." ('049 patent, col. 12:8-11, 16-19) Accordingly, if these moisture-content measurements were incorporated in some way into the constructions for "the α-form crystal" and "the β-form crystal" terms, that would seem to render dependent claims 9 and 11 identical to claims 1 and 3, which is not appropriate. *See, e.g.*, *Boston Sci. Corp. v. Cook Grp. Inc.*, Civil Action No. 15-980-LPS-CJB, 2016 WL 7411128, at *10 (D. Del. Dec. 22, 2016) (explaining that "dependent claims are, by definition, narrower than and include additional limitations as compared to the independent claims") (internal quotation marks and citation omitted); *see also Laitram Corp. v. NEC Corp.*, 62 F.3d 1388, 1392 (Fed. Cir. 1995) ("Although each claim is an independent invention, dependent claims can aid in interpreting the scope of claims from which they depend.").

'containing a description . . . of the thing or things . . . invented or discovered,' which 'shall be so particular' as to 'distinguish the invention or discovery *from other things before known and used*'" and that "[t]he patent laws have retained this requirement of definiteness[.]" *Nautilus*, 134 S. Ct. at 2124-25 (emphasis added). Defendants have not pointed the Court to any case law that indicates otherwise. Therefore, the Court agrees with Plaintiffs that the claims must "distinguish from what is already known, and what is already known [at least on the current, pre-*Markman* hearing record] are two crystalline forms of mirabegron[.]" (Tr. at 41)[14]

Turning then to Defendants' remaining criticism—that the record does not allow a POSA to distinguish the α-form and β-form crystals from *each other*—the Court reverts back to the specification. As was noted above, the written description specifically states that the two forms of crystals "are distinguished from each other by powder X-ray diffraction spectrum and DSC analysis"—that is, that the two forms of crystals are "characterized by [certain] crystal lattice spacings [] of powder X-ray diffraction spectrum and heat absorption peak of DSC analysis." ('049 patent, cols. 1:64-2:19) Thus, it follows that a POSA would understand that "α-form crystal" and "β-form crystal" refers to particular, unique forms of crystals that are, in fact, distinguished "from each other" by certain specific XRPD and DSC peaks disclosed in the

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[14] During the *Markman* hearing, Defendants' counsel asserted, for the first time, that the α-form and β-form crystals are *not* the only known polymorphs of mirabegron. (Tr. at 65, 68) Counsel then handed the Court an international patent application filed by Ranbaxy Laboratories Limited ("Ranbaxy") on March 26, 2015 (the "Ranbaxy application"). (*Id.*) The abstract of this application indicates that the "present invention provides[, *inter alia*,] a crystalline form of mirabegron[.]" World Intellectual Property Organization International Publication Number WO 2015/040605 A1. Yet Defendants did not make this document a part of the pre-*Markman* hearing record. As a result: (1) no expert has testified about the document; (2) Plaintiffs did not have a full and fair opportunity to examine the document before the *Markman* hearing; and (3) there was little substantive discussion about the document during the hearing. (Tr. at 68) For these reasons, the Court declines to consider the document to be a proper part of the record here, and will not consider it further in rendering its decision.

patent. (*See* D.I. 78 at ¶¶ 68-69; Tr. at 38 (Plaintiffs' counsel pointing out that the specification tells the POSA what the characteristics of each crystal form are)); *see also Celgene Corp.*, 2014 WL 2196941, at *4-5 (explaining that a POSA would understand "Form A" to mean a particular polymorph with the observed attributes discussed in the specification as being distinguishable from the other disclosed forms, and construing "Form A" to mean the particular "crystal form describe[d] in the specification as Form A, having all of the characteristics assigned to Form A in the specification").

3. How to Use the Intrinsic Evidence Relating to Exemplar XRPD Spectrums and DSC Heat Absorption Peaks to Demonstrate that One of the Two Crystal Forms at Issue Are Present

From there, the parties seem to dispute *exactly how one must utilize* the above-referenced evidence regarding characteristic XRPD peaks and DSC heat absorption peaks, in order to sufficiently determine whether a sample is the α-form or β-form crystal. This leads to a set of further questions that the Court must answer.

The first of these is whether, in order to confirm the presence of the α-form or β-form crystal, would a POSA rely on DSC measurements *alone* (i.e, not using XRPD testing at all)? (*See* D.I. 77 at 14; D.I. 78 at ¶¶ 74-75 (Dr. Myerson noting that a POSA would understand that "any or all of these various techniques and methodologies [including DSC] may be employed to identify, characterize and distinguish the two crystal forms of mirabegron")) The Court concludes that a POSA would not do so. The specification seems to teach that the POSA would use *both* methodologies (XRPD and DSC), when it explains that these forms are characterized by certain XRPD peaks "*and*" by DSC peaks. Defendants' expert Dr. Craig J. Eckhardt agrees, opining that while DSC is a "well-established technique, in order to conclusively identify a crystal form, DSC should be used in conjunction with another analytical method [here, XRPD

testing]." (D.I. 97 at ¶ 41; *id.* at ¶ 71 (Dr. Eckhardt explaining that "[t]he specification . . . teaches that the 'crystal lattice spacings [] of Tables 1 and 2 *and* heat absorption peak[s] of DSC analysis' should be used together when trying to distinguish the α and β crystal forms from one another") (emphasis in original); *see also id.* at ¶ 57) Even Plaintiffs' expert, Dr. Allan S. Myerson, seemed to agree that a POSA would not (or, at least, that a POSA probably should not) rely on DSC testing alone. Dr. Myerson testified during his deposition that for these crystalline forms, one *could* distinguish between the two forms using only DSC; however, he then quickly added that "more likely you would want to also do X-ray." (D.I. 146, ex. J at 71) At another point in his deposition, when asked how someone carrying out the examples described in the specification would confirm whether his result was the α-form or β-form crystal, Dr. Myerson explained that the POSA "would check using DSC *and* X-ray." (*Id.* at 57 (emphasis added)) Additionally, when asked whether the POSA would use XRPD, DSC and hydroscopic analyses independently or in some combination, in order to distinguish the two crystal forms of mirabegron, Dr. Myerson responded that the POSA "could use X-ray independently or you could use X-ray and DSC together or you could use all of them together." (*Id.* at 68-69)[15] Therefore: (1) the α-form crystal will have a heat absorption peak at 142 to 146° C.; (2) the β-form crystal will have heat absorption peaks at 90 to 110° C. and at 142 to 146° C.; and (3) this DSC testing

[15] In his declaration, Dr. Myerson explained that when the crystal is part of a pharmaceutical composition, the excipients may interfere with the results of a DSC test, and thus the POSA would want to separate the crystal form from the excipients before testing or conduct alternative testing techniques to distinguish the crystal form. (D.I. 78 at ¶ 72) Defendants' counsel addressed this possibility during the *Markman* hearing as well, explaining that when you perform DSC on a tablet, you have many substances inside the tablet that could affect the results. (Tr. at 26)

data must be used in conjunction with characteristic XRPD peak data in order to determine whether one has the relevant crystal form. (*See* D.I. 112 at 3-4)[16]

The second question to be addressed is "How would a POSA use XRPD testing in order to establish that a sample constitutes the α-form or β-form crystal?" Here, the parties argue about how many peaks shown in the x-ray diffractograms for the two crystal forms must be present, in order for a POSA to determine that the sample at issue is either the α-form or β-form crystal.

Dr. Myerson explains that Table 1 (α-form) and Table 2 (β-form) of the patents recite a subset of the peaks that appear in the full XRPD spectra for the two crystal forms. (D.I. 78 at ¶ 58) The full x-ray diffractograms for the two forms are found in Figure 1 (β-form) and Figures 3 and 4 (α-form) of the patents. (*Id.*) Dr. Myerson then focuses on the subsets of peaks that appear in Tables 1 and 2, and asserts that each of these peaks in the respective tables do not overlap with each other. (*Id.*) In other words, each of the peaks for the α-form subset differs from each of the peaks for the β-form subset, and thus "each of those peaks alone is characteristic of the α-form crystal or the β-form crystal for purposes of distinguishing those crystal forms. (*Id.*)[17]

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[16] During the *Markman* hearing, Defendants asserted that a further reason why these claim terms are indefinite is that DSC testing can utilize different configurations of aluminum pans (open, closed or pinhole) that can affect the peaks that result from the testing, yet the patent is silent regarding the type of pan that should be used. (Tr. at 22-25; Defendants' Claim Construction Arguments Presentation, Slides A12, A19) They pointed out that Dr. Myerson seemed to acknowledge the possibility that the type of the pan used can affect testing during his deposition. (D.I. 146, ex. J at 31-32, 59-61) However, this issue was not raised directly in the briefs, (Tr. at 22), and the Court is not now prepared to find that the record contains clear and convincing evidence that these claim terms are indefinite based on the limited arguments made during the *Markman* hearing.

[17] Dr. Myerson explains that when an XRPD analysis is conducted on a

The Court's view is that with regard to the claims at issue in the '049 patent, it is sufficient for a POSA to rely on any number of this subset of "characteristic" XRPD peaks that are unique and distinctive, in order to help characterize a sample of mirabegron crystal as either the α-form or β-form crystal. (Tr. at 40, 42-43)[18] Indeed, Plaintiffs point out that in certain of their ANDA submissions, when representing to the FDA that their mirabegron tablets constituted the α-form or β-form crystal, certain Defendants relied in support on the presence of only some of the subsets of characteristic peaks that are found in Tables 1 and 2 of the patents-in-suit. (D.I. 77 at 14-15; D.I. 155 at 2; D.I. 78 at ¶ 71; Tr. at 48) For example, one Defendant's ANDA documents explained that Astellas' brand name product, Myrbetriq, contained 6 of the 8 XRPD peaks listed in Table 1, and that its generic tablet contained those same 6 peaks, such that the

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pharmaceutical composition that contains both the crystal form and excipients, a POSA would understand that some of the characteristic peaks of the crystal form may be hidden or masked by such excipients, such as if the excipient generates an XRPD peak at the same location as one of the characteristic peaks. (D.I. 78 at ¶ 59)

[18] Defendants point out that the parties have agreed that there is an acceptable amount of variability of ± 0.20 °2Θ as to the measurement of any given peak. As a result, they assert that there is a chance that one of the "characteristic" peaks found in Table 1 and one of the "characteristic" peaks in Table 2 could overlap with the other; this, they claim, would leave a POSA uncertain whether that peak is representative of the α-form or β-form crystal. (D.I. 93 at 11 n.3; D.I. 97 at ¶ 59) More specifically, Table 1 indicates that the α-form crystal has a characteristic peak at 23.16, and Table 2 indicates that the β-form crystal has such a peak at 23.52. (*See, e.g.*, '049 patent at Tables 1-2) If one applied the variation factor of ± 0.20 °2Θ in opposite directions (i.e., by increasing the Table 1/claim 1 peak and decreasing the Table 2/claim 2 peak), then there is a narrow range in which those peaks could overlap (i.e., between 23.32 and 23.36). (*See* D.I. 156 at 4-5; Tr. at 58) Additionally, Defendants' expert asserts that a POSA "would recognize that at least two identified peaks in Table 2 ('β-form crystal[']')[], 19.76 and 22.1, correspond with two peaks in Figures 3 and 4, which are disclosed as representative diffractograms of the α-form crystal." (D.I. 97 at ¶ 59) Plaintiffs respond convincingly, however, that when the POSA conducts an XRPD test, he will get more than just that single peak, and so were this to occur, the POSA would simply rely on the presence of one of the other unique characteristic peaks set out in Table 1 or Table 2 in order to distinguish the crystal form. (Tr. at 53-54, 58; D.I. 146, ex. J at 51-54; D.I. 156 at 5)

generic tablet contained the α-form crystal. (D.I. 79, ex. 13 at 21) Another Defendant indicated that its tablet contained the β-form crystal, and then relied on the presence of 2 of the 5 characteristic XRPD peaks listed in Table 2 for support. (*Id.*, ex. 12) A third Defendant's ANDA submission relies on a single peak listed in Table 1 as indication that the sample contains the α-form crystal. (D.I. 157, ex. 13) This extrinsic evidence helps to confirm that in order to make the relevant identification, a sample need not be shown to include *all* XRPD peaks in the characteristic subsets of peaks listed in Table 1 or Table 2 of the patents. Instead, the sample must simply contain at least one of these "characteristic" XRPD peaks that is unique and distinctive to that form.

In arguing against this conclusion, Defendants contend that the above-referenced ANDA documents are irrelevant because: (1) claim terms must be construed based on their ordinary and customary meaning to a POSA at the time of invention; and (2) the ANDA documents in question were prepared in or around June 2016, 15 years after the alleged priority date of the patents (October 30, 2001). (D.I. 146 at 1-2 (citing cases); Tr. at 13)

The Court does not find the ANDA documents completely irrelevant to the issue, however. Plaintiffs' position (offered via their expert, Dr. Myerson) is clearly that—just as these ANDA filers did 15 years later—a POSA back in 2001 would have been able to utilize a subset of peaks to distinguish one of these crystal samples. (*See* D.I. 78 at ¶ 24 (Dr. Myerson recognizing that patent claim terms are construed from the perspective of a POSA as of the effective filing date of the patent application); *id.* at ¶ 76 (Dr. Myerson citing to these ANDA documents in support of Plaintiffs' construction of these terms)) And Defendants have not sufficiently explained how or why Plaintiffs are wrong—i.e., why a POSA would be able to utilize these peaks for identification purposes in 2016, but would not have been able to do so in

2001. *See, e.g., Mass. Inst. of Tech. v. Shire Pharms, Inc.*, 839 F.3d 1111, 1124 (Fed. Cir. 2016) (rejecting defendant's argument that district court improperly relied on dictionaries from the present day in construing a claim term and finding the term to be definite where "Shire does not explain how . . . dictionaries contemporaneous to the patents' filing date would define the term any differently"); *St. Lawrence Commc'ns LLC v. ZTE Corp.*, CASE NOS. 2:15-CV-349-JRG Lead Case, 2016 WL 6275390, at *66 (E.D. Tex. Oct. 25, 2016) (relying a technical specification identified as "extrinsic evidence" because even though it was not "contemporaneous with the filing of the '521 Patent application, it is nonetheless noteworthy that this technical specification uses the very phrase that Defendants contend is not reasonably certain to a person of ordinary skill in the art"); *Allergan, Inc. v. Sandoz Inc.*, Cause No. 6:11-cv-441, 2013 WL 1314188, at *5 (E.D. Tex. Mar. 28, 2013) (explaining that while the literal scope of a claim term is limited to what it was understood to mean at the time of filing, "documents or data arising after the filing of an application can still be probative to assess the scope of a term at the time of filing").

4. Conclusion

The Court, taking into account all that it has said above, recommends that the term "α-form crystal" be construed to mean "α-form crystal which is a term of reference for a polymorphic crystal form of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide that can be distinguished from other forms by its characteristic peak(s) and DSC analysis as identified in the specification." The Court recommends that the term "β-form crystal" be construed to mean "β-form crystal which is a term of reference for a polymorphic crystal form of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-

phenylethyl)amino]ethyl]acetanilide that can be distinguished from other forms by its characteristic peak(s) and DSC analysis as identified in the specification."

B. "main peaks"

The term "main peaks" appears in claims 1 and 2 of the '117 patent, which are the only two claims in the patent. These claims are reproduced below:

> **1.** A crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2 phenylethyl)amino]ethyl]acetanilide having a heat absorption peak at 142 to 146° C. in the DSC analysis and having *main peaks* at around 5.32, 8.08, 15.28, 17.88, 19.04, 20.20, 23.16 and 24.34 in the terms of 2θ(°) in the powder X-ray diffraction.

('117 patent, col. 12:19-24 (emphasis added) & Certificate of Correction)

> **2.** A crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2 phenylethyl)amino]ethyl]acetanilide having heat absorption peaks at 90 to 110° C. and at 142 to 146° C. in the DSC analysis and having *main peaks* at around 9.68, 19.76, 20.72, 22.10 and 23.52 in the terms of 2θ(°) in the powder X-ray diffraction.

(*Id.*, col. 12:25-30 (emphasis added))

Plaintiffs propose that the term "main peaks" be construed to mean "peaks that are characteristic of the particular crystal form as distinguished from other crystal forms." (D.I. 77 at 3) Defendants argue that the term is indefinite. (D.I. 93 at 3) Alternatively, the ASA Defendants propose that if the Court finds that the term is not indefinite, that the term be construed to mean "peaks with the largest relative intensities in the XRPD spectrum of a sample." (D.I. 95 at 1)

The Court will first address whether the term is indefinite, along with the propriety of Plaintiffs' proposed construction. Thereafter, it will assess the ASA Defendants' proposed construction-in-the-alternative.

1. The Claim Term is Not Indefinite and Plaintiffs' Proposed Construction Is Supported by the Intrinsic Record

It is undisputed that the term "main peaks" is not a term of art applied by POSAs in this field. (D.I. 97 at ¶ 45; D.I. 155 at 5) Thus, to discern the meaning of the term, the POSA would need to turn to the intrinsic evidence. (*See* D.I. 155 at 5 (Plaintiffs explaining that there is not "some art-established meaning" for the term and thus "its meaning is derived from the claim language and the patent specification")); *see also, e.g.*, *Astra Aktiebolag v. Andrx Pharms., Inc.*, 222 F. Supp. 2d 423, 451 (S.D.N.Y. 2002) (explaining that, with respect to a term that the "patentees created for use" in the asserted patents, such term "must be defined in the context of those patents" and accordingly the "court must rely on the intrinsic evidence, particularly the specification, to determine the meaning of the [term]").

The specification of the '117 patent (which is identical to that of the '049 patent) explains that:

> *Each of the α-form crystal and the β-form crystal is characterized by the following crystal lattice spacings* [20(°)] of powder X-ray diffraction spectrum and heat absorption peak of DSC analysis. Incidentally, with respect to the powder X-ray diffraction, in determining the identity of crystal, crystal lattice spacings and an overall pattern are important in the nature of data. On the other hand, since a relative intensity can vary a little depending upon the direction of crystal growth, particle size and measurement condition, it should not be strictly interpreted.

('117 patent, col. 2:6-15 (emphasis added)) The patent then provides Table 1 and Table 2, which are depicted above, *supra* at 15. As was previously noted above, the peaks listed in each table (8 for α-form crystal and 5 for the β-form crystal) constitute only a selected subset of XRPD peaks that appear in the full X-ray diffractograms for the α-form crystal (found in Figures 3 and 4 of

the patent) and the β-form crystal (found in Figure 1 of the patent), respectively. (*See id.*, FIGS. 1, 3, 4; D.I. 78 at ¶ 58; D.I. 77 at 6)

Importantly, as Plaintiffs explain, these subsets of peaks in Tables 1 and 2—those listed in the Tables as being characteristic of the "α-form Crystal" and the "β-form Crystal"—*are the same peaks that are listed in claims 1 and 2 of the '117 patent* and that are described in those claims as "main peaks." Plaintiffs' proposed construction, then, is gleaned directly from the intrinsic record—Plaintiffs emphasize that the "main peaks" listed in the claims are the very "peaks that are characteristic of the particular crystal form as distinguished from other crystal forms." (*See* D.I. 77 at 6; D.I. 155 at 5 ("Defendants do not dispute that Tables 1 and 2 of the '117 Patent specification list the same eight peaks that appear in Claim 1, and the same five peaks that appear in Claim 2, or that the accompanying text describes them as the ones that 'characterize' the two novel crystalline forms.")) Plaintiffs explain that the word "main" in the claim is simply meant to emphasize that while there are other peaks in the full x-ray diffractograms for both of the crystalline forms, the listed peaks are the ones the patentee took care to identify as those characterizing the two crystalline forms that are the invention. (D.I. 112 at 5 ("[T]he claim term 'main' informs the POSA that the peaks recited in the claims are peaks that appear within an XRPD diffractogram that may also contain additional peaks for the claimed crystal forms" and that the identified peaks "can be used to 'characterize' the two crystalline forms"); Tr. at 105-08; *see also* D.I. 146, ex. J at 62 (Dr. Myerson testifying that "[c]haracteristic peaks are the set of peaks you pick to characterize your sample, which in the case of the '117 [patent] are the peaks listed. . . . You can pick any set of peaks that allows you to characterize"); *id.* at 11 (Dr. Myerson explaining that "[c]haracteristic peaks are normally listed as peaks that can be used to characterize a form . . . . You can pick any set that allows you to characterize the

compound"))[19] In view of the intrinsic record, then, the Court agrees with Plaintiffs that "main peaks" should be construed to mean "peaks that are characteristic of the particular crystal form as distinguished from other crystal forms."

In coming to this conclusion, the Court rejects Defendants' argument that the term "main peaks" is indefinite. In Defendants' view, "[t]he intrinsic record provides no guidance as to whether 'main peaks' refers to XRPD peaks that are unique to each mirabegron crystal form." (D.I. 93 at 4) This argument, however, rests on the flawed premise that there is no connection between the claimed "main peaks" and the α-form crystal and the β-form crystals of mirabegron. According to Defendants, because (1) the claims of the '117 patent do not use the words "α-form crystal" and "β-form crystal" and (2) the specification does not explicitly state that there is any relationship between the claims, Tables 1 and 2 or Figures 1, 3 and 4, then (3) the POSA would understand that "the recited 'main peaks' do *not* refer to and are *not* constrained by the particular XRPD diffractograms [of the α-form crystal and β-form crystal] illustrated in the Figures or Tables." (*Id.* at 5 (emphasis added)); *see also* Tr. at 88)

The assertion that claims 1 and 2 relate to something other than the α-form crystal and β-form crystal is puzzling. There is a clear relationship between Table 1 (which states that it relates to the "α-form crystal") and Table 2 (which states that it relates to the "β-form crystal") on the one hand, and the peaks recited in claims 1 and 2 on the other. The Tables and the claims

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[19] Indeed, in arguing for an alternative construction of "main peaks" that would have the term relate to relative intensity, the ASA Defendants attached the dictionary definition of "main," which is defined therein as "chief in size, extent, or importance; principal; leading[.]" (D.I. 96, ex. A at 1159) The "chief in . . . importance" aspect of this definition certainly comports with Plaintiffs' proposed construction; these "main" peaks are the subset that the patentees have identified as characteristic of the crystal forms—they are thus "chief in importance" among all peaks located in the full diffractograms for these crystal forms.

both list out the very same peaks. Moreover, claims 1 and 2 are the only two claims in a patent that is entitled "α-Form or β-Form Crystal of Acetanilide Derivative." Indeed, the specification explains that "[t]he present invention relates to an *α-form crystal or β-form crystal* of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]-acetanilide[.]" ('117 patent, col. 1:6-10 (emphasis added); *see also* Tr. at 110)[20] "Claim terms are not construed in a vacuum divorced from the specification[,]" *Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1290 (Fed. Cir. 2010), and here the patent is telling us that these *are* claims to the α-form crystal (claim 1) and β-form crystal (claim 2), respectively.

Defendants' related assertion that "the specification never explains the relationship, if any, between the Figures and the Tables[,]" (D.I. 93 at 5), is also a head-scratcher. The

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[20] One of Defendants' assertions here seems to be that since the applicants used the term "characterized by" in the specification when referring to the peaks listed in Table 1 and Table 2 (i.e., in explaining how the two crystal forms were "characterized by" the peaks listed in these Tables), then the term "main peaks" in the claims must be meant to refer to something additional other than simply being a reference to these "characteristic peaks." Defendants' argument is that "if the applicants wanted to claim 'characteristic' peaks, they knew how to do so." (D.I. 146 at 7) However, the Federal Circuit has explained that "it is not unknown for different words to be used to express similar concepts." *Bancorp Servs., L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1373 (Fed. Cir. 2004). Defendants' argument might have more force if, for example, there were other claims in the patent that used the term "characteristic" instead of "main." Or it might be a stronger argument if the situation were more like that in a case cited by Defendants: *Novartis Pharm. Corp. v. Actavis, Inc.*, Civil Action No. 12-366-RGA-CJB, 2013 WL 6142747, at *5-6 (D. Del. Nov. 21, 2013). (D.I. 146 at 7) In *Novartis*, the patentees used both the term "disorders" and the term "diseases" in the specification—the former to refer to a broad category of maladies, and the latter to refer to a narrower group of ills. *Id.* Since the claims used the term "diseases" (and not "disorders") and since the patentee had used both terms in the specification to mean different things, that all suggested that the construction of the claim term "diseases" should not incorporate the word "disorders." *Id.* Here, in contrast, while the specification does use the phrase "characterized by" to describe certain peaks, it never uses the term "main" at all. And so it seems much more plausible here (as opposed to the situation in *Novartis*) that the patentee used "main peaks" in the claims as a kind of synonym for the "character[istic]" peaks set out in Tables 1 and 2.

specification clearly explains that Figures 1, 3 and 4 depict powder X-ray diffraction diagrams for the α-form crystal (Figures 3 and 4) and the β-form crystal (Figure 1). ('117 patent, col. 11:9-12, 16-23) And Tables 1 (α-form crystal) and 2 (β-form crystal) set out a subset of peaks found in these full diffractograms—the peaks that are said to "characterize[]" the α-form crystal and the β-form crystals, respectively. These are the exact same peaks that are described as "main peaks" for the crystals claimed in claims 1 and 2 of the '117 patent.[21]

Therefore, the Court agrees with Plaintiffs that "main peaks" is not indefinite, and that a POSA "would easily be able to ascertain whether a mirabegron crystal form conforms to the claims of the '117 patent by, for example, testing it by XRPD and then determining whether peaks are present at the recited locations." (D.I. 112 at 5) If they are, and if the form also displays the heat absorption peaks recited in the claims, "then the claim limitations are met, irrespective of any relative intensities or whether additional peaks are also present in the XRPD diffractogram." (*Id.*)[22]

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[21] The Court further notes that claim 1, which recites "main peaks" that are the same as those listed in Table 1 as characterizing the α-form crystal, further recites that the claimed crystal has a heat absorption peak at 142 to 146° C. in the DSC analysis. ('117 patent, col. 12:19-24) Claim 2, which recites "main peaks" that are the same as those listed in Table 2 as characterizing the β-form crystal, further recites that the claimed crystal has heat absorption peaks at 90 to 110°C. and at 142 to 146° C. in the DSC analysis. (*Id.*, col. 12:25-30) Immediately before the inclusion of Tables 1 and 2, the specification explains that the novel α-form and β-form crystals of the present invention are distinguished from one another by, *inter alia*, DSC analysis. And it goes on to state immediately after the Tables that "in the DSC analysis, the α-form crystal had a heat absorption peak at 142 to 146° C., and the β-form crystal had heat absorption peaks at 90 to 110°C. and at 142 to 146° C., respectively." (*Id.*, col. 2:38-41) In the Court's view, this further underscores that the claims 1 and 2 are clearly directed to the α-form crystal and the β-form crystal, respectively.

[22] Defendants also argue that claimed "main peaks" do not distinguish one polymorphic form of mirabegron from another. First, they contend, when one considers the full diffractograms set out in Figures 3 and 4 for the α-form crystal and Figure 1 for the β-form crystal, that both forms show peaks at about (within ± 0.2 °20) 17.0, 18.6, 19.8, 22.0, 25.0, 25.8,

2. The ASA Defendants' Proposed Construction is Flawed

Before concluding, the Court pauses to address the ASA Defendants' alternative request that, if the Court were to find that "main peaks" should be construed, the correct construction is "peaks with the largest relative intensities in the XRPD spectrum of a sample." (D.I. 95 at 1) The ASA Defendants explain that the term "main" must "add something to the claims—it must modify *what types* of peaks are found at the" recited locations. (*Id.* (emphasis in original)) Construing "main" as they propose would be consistent with the intrinsic record, the ASA Defendants argue, because Tables 1 and 2 list both the characteristic peaks' locations *and* their "[r]elative intensity." (*Id.* at 2; *see also* '117 patent, col. 2:16-37) Lastly, the ASA Defendants contend that this proposal is consistent with the extrinsic evidence, such as other patents filed at the relevant time that use "main peaks" to refer to intensity of peaks in a given spectrum. (D.I. 95 at 2-3 & n.4; Tr. at 96-97, 99) The Court, however, is not persuaded.

Taking up the latter argument (regarding extrinsic evidence) first, the Court reiterates what the parties have all agreed on—that the term "main peaks" is *not* a term of art typically used by POSAs when analyzing X-ray diffraction patterns. (D.I. 97 at ¶ 45; D.I. 155 at 5) If that is so, then the term's meaning must be gleaned from the *intrinsic record.* How the term may

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and 29.2, thus rendering any single peak location useless in distinguishing polymorphs. (D.I. 93 at 9) And second, Defendants note that the number of XRPD peaks required to uniquely identify a polymorphic form can vary depending on the sample tested. (*Id.*; *see also* D.I. 97 at ¶ 36) Defendants' position disregards that Plaintiffs' proposed construction for claims 1 and 2 requires the presence of the *entire set* of peaks in the claim in order to distinguish the claimed form. (D.I. 112 at 6 ("Defendants ignore that what the specification describes is two sets of peaks that respectively characterize the two crystalline forms[.]"); D.I. 155 at 5; *id.* at 7 n.5 (indicating that the '117 patent claims "require all the recited XRPD peaks, not just one"); Tr. at 104 (Plaintiffs' counsel acknowledging that "in order to prove infringement, we have to prove the presence of each one of those peaks")) Defendants do not appear to dispute that, taking the peaks recited in each claim of the '117 patent as a set, those peaks together are unique sets. (*See* Tr. at 102-03, 106)

have been defined in other patents is not of great relevance to the correct construction here. (*See* Tr. at 113-14)

Additionally, the Court disagrees with the ASA Defendants' assertion that their proposal is consistent with the intrinsic record. Indeed, for at least two reasons, the '117 patent's specification does not support a construction of "main peaks" that links those peaks with the "largest relative intensities."

First, while it is true that Tables 1 and 2 include columns relating to relative intensities (as well as columns listing crystal lattice spacings), the specification states that the crystal forms are "characterized by the following *crystal lattice spacings*" and "heat absorption peak of DSC analysis." ('117 patent, col. 2:6-9 (emphasis added)) It does *not* state that the crystal forms are "characterized by the following crystal lattice spacings, *relative intensities*, and DSC heat absorption peaks." And the specification informs the POSA that:

> [W]ith respect to the powder X-ray diffraction, in determining the identity of crystal, crystal lattice spacings and an overall pattern are important in the nature of data. On the other hand, since a relative intensity can vary a little depending upon the direction of crystal growth, particle size and measurement condition, it *should not be strictly interpreted.*

(*Id.*, col. 2:9-15 (emphasis added)) Thus, the import of the specification, in the Court's view, is that relative intensity is *not* what allows a POSA to distinguish crystalline forms from one another. Rather, it is a set of distinguishing peaks that allows a POSA to do so. (D.I. 112 at 7-9; Tr. at 108-10)[23]

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[23] The ASA Defendants criticize Plaintiffs for putting forward a construction that "essentially reads the word 'main' out of the claims" because "the location . . . of the peaks, which is what Plaintiffs argue makes a peak 'characteristic . . . as distinguished from other crystal forms,' is already covered by the specific °20 values in each claim." (D.I. 95 at 1-2) The Court acknowledges the ASA Defendants' point, in the sense that under Plaintiffs' reading, if the

Second, one of the XRPD peaks in the full diffractogram in Figure 1 (which corresponds to the β-form crystal) is not listed in claim 2 (which claims the same peaks and DSC peaks as those that distinguish the β-form crystal)—and yet that peak is more intense than one of the "main peaks" recited in the claim. (D.I. 77 at 8; D.I. 112 at 8; D.I. 78 at ¶ 63) Figure 1 shows an intense peak at approximately 22.5, which is not recited in Claim 2, whereas Claim 2 recites a peak at 9.68 that is less intense than the peak at 22.5. ('117 patent, FIG. 1 & col. 12:25-30) Therefore, as Plaintiffs summarize, "[f]or the ASA Defendants' construction to make sense, claim 2 would have to have recited the peak at 22.5 because this peak is more intense than at least one other peak that is recited in claim 2 (9.68). Its absence confirms that 'main peaks' cannot mean most intense peaks." (D.I. 77 at 8)

3. Conclusion

For the foregoing reasons, the Court recommends that the term "main peaks" be construed to mean "peaks that are characteristic of the particular crystal form as distinguished from other crystal forms."

C. "contains less than 0.2% of moisture" and "contains less than 3% of moisture"

The disputed term "contains less than 0.2% of moisture" appears in dependent claim 9 of the '049 patent, which depends from claim 1. The disputed term "contains less than 3% of moisture" appears in dependent claim 11 of the '049 patent, which depends from claim 3.

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word "main" were removed from the claims, the claims' meaning would be no different than if the word remained in the claims. In both scenarios, the XRPD peaks at issue are the same peaks that are later specified numerically in the claims. (D.I. 146, ex. J at 144) That said, for the reasons previously set out above, the Court ultimately concludes that the word "main" is being used in the claims for emphasis. It is used descriptively, in order to make clear that the numeric peaks thereafter referenced in the claims are very important tools used to identify what it is that makes up these crystal forms.

Claims 9 and 11 are reproduced below (claims 1 and 3 were already reproduced above in connection with the discussion of the "α-form crystal" and "β-form crystal" terms):

> **9.** The pharmaceutical composition of claim **1**, wherein the α-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide *contains less than 0.2 % of moisture.*

('049 patent, col. 12:8-11 (emphasis added))

> **11.** The pharmaceutical composition of claim **3**, wherein the β-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide *contains less than 3% of moisture.*

(*Id.*, col. 12:16-19 (emphasis added))

Plaintiffs propose that the term "contains less than 0.2% of moisture" be construed to mean "the α-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide used to prepare the pharmaceutical composition contains less than 0.2% moisture." (D.I. 77 at 16) Similarly, Plaintiffs propose that the term "contains less than 3% of moisture" be construed to mean "the β-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide used to prepare the pharmaceutical composition contains less than 3% moisture." (*Id.*) Meanwhile, Defendants assert that these terms are indefinite. (*Id.*)

The crux of the dispute relates to when the moisture content measurement called for in these claim terms is measured. Independent claims 1 and 3, on which claims 9 and 11 depend, claim a "solid pharmaceutical composition" that is made of 2 components (mirabegron and a "pharmaceutically acceptable carrier"). ('049 patent, col. 11:5-8, 14-17) The disagreement here is over whether the moisture content of the crystal mirabegron is to be measured before the crystal mirabegron is formulated into a final solid composition, or whether the moisture content

of the crystal mirabegron is to be measured after the crystal mirabegron is part of the final solid composition (i.e., combined with the pharmaceutically acceptable carrier)?

Defendants assert that the answer is the latter, which, they further argue, renders the claims indefinite. This is so, they assert, in light of claims 9 and 11's dependence on claims 1 and 3, respectively. Claims 1 and 3 make it clear that claims 9 and 11 are directed to final, "solid pharmaceutical composition[s]" (comprising mirabegron crystals and one or more excipients). Therefore, Defendants' argument goes, the claimed moisture content of mirabegron refers to a moisture content measurement taken of mirabegron *when it is part of the pharmaceutical composition.* (D.I. 93 at 17; D.I. 146 at 10; Tr. at 117-19) Yet Defendants assert that the intrinsic record does not teach (and a POSA would not know) how to determine the moisture content of the mirabegron portion of the final dosage form as claimed by claims 9 and 11. (D.I. 93 at 17; D.I. 146 at 10; Tr. at 117-19)

In support, Defendants rely on their expert, Dr. Eckhardt, who opines that while there are methods for determining the overall moisture content of a final, solid composition, there would be no way for the POSA to determine whether that measurement is attributable to the mirabegron component of the composition, or instead to some other excipient within the composition. (D.I. 97 at ¶ 82)[24] Dr. Eckhardt points out that the specification of the '049 patent "apparently describes only moisture content testing of mirabegron *before* it is formulated into a composition." (*Id.* (emphasis in original) (citing '049 patent, col. 9:31-67))

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[24] Plaintiffs' expert, Dr. Myerson, does not appear to vigorously dispute this fact. (D.I. 78 at ¶ 86)

Plaintiffs, meanwhile, argue that the moisture content measurements are made on the crystal form itself, which is *then* used to produce the claimed pharmaceutical composition. (D.I. 77 at 16) For the reasons that follow, the Court agrees with Plaintiffs.

Turning first to the claim language, the Court concludes that it is not unreasonable to read claims 9 and 11 as Plaintiffs suggest. (*See* Tr. at 128; D.I. 77 at 18 ("In dependent claims 9 and 11, the moisture content is defined for just the crystal form of the active ingredient, not the entire pharmaceutical composition[.]"); D.I. 78 at ¶ 83) In other words, the Court has not been persuaded that a reading of claims 1 and 9 as follows, for example, is wrong:

> **1/9**. A solid pharmaceutical composition comprising the α-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide [that "contains less than 0.2% of moisture before it has been introduced into the pharmaceutical composition"] and a pharmaceutically acceptable carrier.

Such a reading conveys that two components go into making up the solid pharmaceutical composition: (1) an α-form crystal that contains less than 0.2 % of moisture; and (2) a pharmaceutically acceptable carrier.[25]

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[25] The Court notes that other dependent claims 5 and 7 are structured in the same way as claims 9 and 11 in reciting "[t]he pharmaceutical composition of claim [1 and 3;]" these dependent claims go on to address aspects of the *other component* used to make up the solid final dosage form, i.e., the "pharmaceutically acceptable carrier." Claim 5, for example, recites "[t]he pharmaceutical composition of claim **1**, wherein the pharmaceutically acceptable carrier is selected from a group consisting of lactose, mannitol, glucose, hydroxypropyl cellulose, microcrystalline cellulose, starch, polyvinylpyrolidone, and magnesium metasilicate aluminate." ('049 patent, col. 11:23-27) In the Court's view, these dependent claims further support Plaintiffs' position that their proposed constructions are perfectly reasonable ways to interpret the claims. That is, similar to how claims 5 and 7 narrow the field of the "pharmaceutically acceptable carrier" component that is to be used in the final solid pharmaceutical composition, claims 9 and 11 further define the crystal component that is to be used in the final solid pharmaceutical composition. And claims 9 and 11 do so by requiring that crystal component to have a moisture content of less than 0.2% or less than 3%, respectively, before formulation.

Importantly, Plaintiffs' interpretation of these claims terms (as relating to the moisture content of the crystal mirabegron *before* it is combined with a pharmaceutically acceptable carrier to formulate a "solid pharmaceutical composition") is wholly consistent with the '049 patent specification. (D.I. 77 at 17-18) As even Defendants' expert recognized, the specification discusses moisture content testing carried out on the crystal mirabegron itself—mirabegron that is *then* used to formulate the pharmaceutical composition. (D.I. 97 at ¶ 82; *see also* D.I. 77 at 16-17; D.I. 112 at 10) With respect to the α-form crystal of mirabegron (at issue in claims 1 and 9), the specification explains that the hygroscopicity of the α-form crystal of the invention was measured "using VTI SGA-100" under particular conditions, and "[a]s a result . . . . the α-form crystal of the invention had a moisture-holding amount of not more than 0.2% over the entire range of relative humidity from 5% to 95% and did not exhibit hygroscopicity (see FIG. **9**)." ('049 patent, col. 9:42-54; D.I. 77 at 17; D.I. 78 at ¶ 81) Likewise, using the same test under the same conditions, the patentee reported that "in the β-form crystal, an increase in the weight was observed from a relative humidity of about 20%, and it held moisture of about 3% and exhibited weak hygroscopicity (see FIG. **8**)." ('049 patent, col. 9:42-57; D.I. 77 at 17; D.I. 78 at ¶ 82) Figures 9 and 8 of the '049 patent depict hygroscopicity curve diagrams of the α-form and β-form crystals, respectively. ('049 patent, col. 10:57-64; D.I. 78 at ¶¶ 81-82) The patentees then note that the "α-form crystal of the invention does not exhibit hygroscopicity and is excellent in stability, and therefore, is suitable as a starting material for the production of medicines." ('049 patent, col. 9:62-65) As for the β-form crystal, the patentees explain that it "has weak hygroscopicity" but "is a metastable-form crystal and can be used as a medicine." (*Id.*, col. 9:65-67) Thus, the specification clearly demonstrates that the moisture content of the mirabegron

crystal that is found in a solid dosage form is measured "by itself before it has been introduced into a pharmaceutical composition." (D.I. 112 at 10)

Lastly, such a reading of the claims is also consistent with the undisputed fact there is and was no way to reliably test the final, solid composition in order to obtain the moisture content of the crystal component alone. Any attempt to do so would result in a measurement of the moisture present in *both* the crystal form and in the excipients. (D.I. 77 at 19; D.I. 78 at ¶ 86; D.I. 97 at ¶ 83) It does not make sense that the patentee would write the claims in such a way so as to require that a measurement (i.e., that of the moisture content of the crystal form alone) be taken at a point in time (i.e., when the crystal form is combined with excipients) when obtaining that very measurement would be nearly impossible. (Tr. at 122 (Defendants' counsel acknowledging that interpreting these claim terms as Defendants propose would render the claims "[n]onsensical[,]" in that the claims would require measurements that are unobtainable, but arguing that this is what the claim language literally requires))

For these reasons, the Court finds that the claim language and specification is consistent with Plaintiffs' proposed construction.[26] The Court will tweak that proposed construction

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[26] Defendants assert that the circumstances here are "on all fours" with the Federal Circuit's decision in *Chef Am., Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371 (Fed. Cir. 2004). (Tr. at 119; *see also* D.I. 93 at 20) In that case, the relevant claim recited a method for baking cookies and required "heating the resulting batter-coated dough to a temperature in the range of about 400° F. to 850° F." 358 F.3d at 1373. Because the claim language "unambiguously require[d] that *the dough* be heated to a temperature range of 400° F to 850° F[,]" as opposed to requiring that *the oven in which the dough is cooked* be heated to this range, the Federal Circuit construed the claim as such—even though carrying out such a method would burn the dough to a crisp. *Id.* at 1373-74 (emphasis added). The Court explained that the claim contained "ordinary, simple English words whose meaning is clear and unquestionable" and that, accordingly, it must "construe the claim as written, not as the patentees wish they had written it." *Id.*

The Court finds the instant scenario to be distinguishable from *Chef America.* Here, the claim language, standing alone, could be reasonably interpreted as both parties posit. And so the

slightly, simply to better emphasize that the moisture content of the crystal is tested before the crystal is introduced into the pharmaceutical composition. It therefore recommends that the term "contains less than 0.2% of moisture" be construed to mean "the α-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide used to prepare the pharmaceutical composition contains less than 0.2% moisture before it has been introduced into the pharmaceutical composition." The Court likewise recommends that the term "contains less than 3% of moisture" be construed to mean "the β-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide used to prepare the pharmaceutical composition contains less than 3% moisture before it has been introduced into the pharmaceutical composition."

IV. CONCLUSION

For the foregoing reasons, the Court recommends that the District Court adopt the following constructions:

1. "α-form crystal" should be construed to mean "α-form crystal which is a term of reference for a polymorphic crystal form of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide that can be distinguished from other forms by its

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Court's decision does not amount to re-writing the claim language. Instead, the Court's decision was driven by a determination of which construction makes the most sense, in light of the intrinsic and extrinsic evidence of record. *See, e.g.*, *Akzo Nobel Coatings, Inc. v. Dow Chem. Co.*, 811 F.3d 1334, 1344-45 (Fed. Cir. 2016) (explaining that *Chef America* was distinguishable where the Federal Circuit's affirmance of the district court's claim construction did not amount to re-drafting the claims, but rather "construing the claims to require the heightened temperature range to apply to the elevated temperature phases in accordance with the specification"); *Eidos Display, LLC v. AU Optronics Corp.*, 779 F.3d 1360, 1367-68 (Fed. Cir. 2015) ("Determining how a person of ordinary skill in the art would understand the limitation, however, is different from rewriting the limitation.").

characteristic peak(s) and DSC analysis as identified in the specification" and "β-form crystal" should be construed to mean "β-form crystal which is a term of reference for a polymorphic crystal form of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide that can be distinguished from other forms by its characteristic peak(s) and DSC analysis as identified in the specification"

2. "main peaks" should be construed to mean "peaks that are characteristic of the particular crystal form as distinguished from other crystal forms"

3. "contains less than 0.2% of moisture" should be construed to mean "the α-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide used to prepare the pharmaceutical composition contains less than 0.2% moisture before it has been introduced into the pharmaceutical composition" and "contains less than 3% of moisture" should be construed to mean "the β-form crystal of (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide used to prepare the pharmaceutical composition contains less than 3% moisture before it has been introduced into the pharmaceutical composition"

This Report and Recommendation is filed pursuant to 28 U.S.C. § 636(b)(1)(B), Fed. R. Civ. P. 72(b)(1), and D. Del. LR 72.1. The parties may serve and file specific written objections within fourteen (14) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b)(2). The failure of a party to object to legal conclusions may result in the loss of the right to de novo review in the district court. *See Henderson v. Carlson*, 812 F.2d 874, 878-79 (3d Cir. 1987); *Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1 (3d Cir. 2006).

The parties are directed to the Court's Standing Order for Objections Filed Under Fed. R. Civ. P. 72, dated October 9, 2013, a copy of which is available on the District Court's website, located at http://www.ded.uscourts.gov.

Because this Report and Recommendation may contain confidential information, it has been released under seal, pending review by the parties to allow them to submit a single, jointly proposed, redacted version (if necessary) of the Report and Recommendation. Any such redacted version shall be submitted no later than **June 21, 2018,** for review by the Court, along with a motion for redaction that includes a clear, factually detailed explanation as to why disclosure of any proposed redacted material would "work a clearly defined and serious injury to the party seeking closure." *Pansy v. Borough of Stroudsburg*, 23 F.3d 772, 786 (3d Cir. 1994) (internal quotation marks and citation omitted). The Court will subsequently issue a publicly-available version of its Report and Recommendation.

Dated: June 18, 2018

Christopher J. Burke
UNITED STATES MAGISTRATE JUDGE