IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
TORRENT PHARMACEUTICALS LIMITED, INC., TORRENT PHARMA INC., and HETERO LABS LIMITED,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
ALEMBIC PHARMACEUTICALS LIMITED, ALEMBIC LIMITED, ALEMBIC GLOBAL HOLDING SA, and ALEMBIC PHARMACEUTICALS INC.,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
ZYDUS PHARMACEUTICALS USA, INC. and CADILA HEALTHCARE LIMITED,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
AUROBINDO PHARMA LIMITED, AUROBINDO PHARMA USA, INC., and AUROLIFE PHARMA LLC,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
INTAS PHARMACEUTICALS LIMITED, ACCORD HEALTHCARE, INC., and HETERO LABS LIMITED,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
SUN PHARMACEUTICAL INDUSTRIES LTD., SUN PHARMA GLOBAL INC., SUN PHARMA GLOBAL FZE, SUN PHARMA USA, SUN PHARMACEUTICALS INDUSTRIES, INC., and CARACO PHARMACEUTICAL LABORATORIES,
Defendants.

HONORABLE JEROME B. SIMANDLE

Civil Action Nos.
14-1078 (JBS/KMW)
14-2982 (JBS/KMW)
14-3168 (JBS/KMW)
14-3306 (JBS/KMW)
14-3996 (JBS/KMW)
14-4307 (JBS/KMW)
14-4508 (JBS/KMW)
14-4671 (JBS/KMW)
14-5537 (JBS/KMW)
14-5876 (JBS/KMW)
14-5878 (JBS/KMW)
14-6158 (JBS/KMW)
14-6397 (JBS/KMW)
14-6398 (JBS/KMW)
14-6890 (JBS/KMW)
14-7105 (JBS/KMW)
14-7252 (JBS/KMW)
14-7405 (JBS/KMW)
14-8074 (JBS/KMW)
14-8077 (JBS/KMW)
15-1585 (JBS/KMW)
15-161 (JBS/KMW)

MARKMAN OPINION

[Caption Continues]

OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. MYLAN, INC., MYLAN PHARMACEUTICALS INC., and MYLAN LABORATORIES LIMITED, Defendants.
OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. TORRENT PHARMACEUTICALS LIMITED, INC., TORRENT PHARMA INC., and HETERO LABS LIMITED, Defendants.
OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. ZHEJIANG HUAHAI PHARMACEUTICAL CO., LTD., HUAHAI US INC., PRINSTON PHARMACEUTICAL INC., and SOLCO HEALTHCARE U.S., LLC, Defendants.
OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. AJANTA PHARMA LIMITED and AJANTA PHARMA USA INC., Defendants.
OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. TEVA PHARMACEUTICALS USA, INC., Defendant.
OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. INTAS PHARMACEUTICALS LIMITED, ACCORD HEALTHCARE, INC., and HETERO LABS LIMITED, Defendants.
OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. SUN PHARMACEUTICAL INDUSTRIES LTD., SUN PHARMA GLOBAL INC., SUN PHARMA GLOBAL FZE, SUN PHARMA USA, SUN PHARMACEUTICALS INDUSTRIES, INC., and CARACO PHARMACEUTICAL LABORATORIES, Defendants.

[Caption Continues]

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
TEVA PHARMACEUTICALS USA, INC.,
Defendant.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
AUROBINDO PHARMA LIMITED, AUROBINDO PHARMA USA, INC., and AUROLIFE PHARMA LLC,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
LUPIN LIMITED, LUPIN ATLANTIS HOLDING SA, LUPIN PHARMACEUTICALS, INC., and HETERO LABS LIMITED,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
ZYDUS PHARMACEUTICALS USA and CADILA HEALTHCARE LIMITED,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
ALEMBIC PHARMACEUTICALS LIMITED, ALEMBIC LIMITED, ALEMBIC GLOBAL HOLDING SA, and ALEMBIC PHARMACEUTICALS INC.,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
APOTEX CORP., APOTEX INC., APOTEX PHARMACHEM INC., and HETERO LABS LIMITED,
Defendants.

OTSUKA PHARMACEUTICAL CO., LTD.,
Plaintiff,
v.
SCIEGEN PHARMACEUTICALS INC. and BACTOLAC PHARMACEUTICAL, INC.,
Defendants.

[Caption Continues]

OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS INDIA PVT. LTD., MSN PHARMACHEM PVT. LTD., and MSN LABORATORIES PVT. LTD., Defendants.
OTSUKA PHARMACEUTICAL CO., LTD., Plaintiff, v. HETERO DRUGS LIMITED, HETERO LABS LIMITED, and HETERO USA, INC., Defendants.

SIMANDLE, Chief Judge:

Table of Contents

I. INTRODUCTION

These related patent infringement actions under the Hatch-Waxman Act, 35 U.S.C. §§ 271, 281, generally concern Plaintiff Otsuka Pharmaceutical Co, Ltd.'s (hereinafter, "Otsuka") position that Defendants' submissions of abbreviated new drug applications (hereinafter, "ANDAs") infringe the various patents covering Otsuka's Abilify® aripiprazole product, U.S. Patent Nos. 5,006,528 ("the '528 patent"), 7,053,092 ("the '092 patent"), 8,017,615 ("the '615 patent"), 8,580,796 ("the '796 patent"), 8,642,600 ("the '600 patent"), 8,642,760 ("the '760 patent"), and 8,759,350 ("the '350 patent" and collectively, the "patents-in-suit").

Following Otsuka's preliminary injunction motion practice, see Otsuka Pharm. Co., Ltd. v. Torrent Pharm. Ltd., Inc., ___ F. Supp. 3d ____, 2015 WL 1782653 (D.N.J. Apr. 16, 2015), and the parties' lengthy period for claims construction discovery (marked by a plethora of discovery disputes and discovery motion practice before this Court),[1] the parties now request that the Court construe the following five claim phrases:

[1] For example, on September 25, 2015, this Court granted in part and denied in part Otsuka's motions to strike certain portions of Defendants' responsive Markman expert declarations, See

1. "**Anhydrous Aripiprazole Crystals B**," as it appears in asserted claims 3, 4, 15, and 16 of the '615 Patent, claims 1 and 2 of the '796 Patent, and claims 4 and 12 of the '350 Patent;

2. "**mean particle size**," as it appears in asserted claims 3, 4, 15, and 16 of the '615 Patent;

3. "**wherein said low hygroscopicity is defined as a moisture content of [0.40%/0.10%] or less after placing said substance/Crystals for 24 hours in a desiccator maintained at a temperature of 60° C and a humidity level of 100%**," as it appears in asserted claims 3, 4, 15, and 16 of the '615 Patent, claims 1 and 2 of the '796 Patent, and claims 1 and 2 of the '760 Patent;

4. "**aripiprazole drug substance**," as it appears in asserted claims 1 and 2 of the '760 Patent;[2] and

5. "**a/the pharmaceutical composition**" / "**in combination with**," as it appears in asserted claims 1 through 18 of the '350 Patent.

Otsuka, for its part, largely eschews the need for formal claim construction and submits, in each instance, that the disputed claim phrase should be construed in accordance with its plain and ordinary meaning as understood by a person of ordinary skill in the art. (See, e.g., Otsuka's Opening Claim Constr. Br

---

Otsuka Pharm. Co., Ltd. v. Torrent Pharms. Ltd., Inc., ___ F. Supp. 3d ____, 2015 WL 5665771 (D.N.J. Sept. 25, 2015), and then separately denied Defendants Apotex Corp.'s and Apotex Inc.'s motion for a protective order barring any additional deposition of Graham Buckton, Ph.D (hereinafter, "Dr. Buckton" or "Dr. Graham Buckton"). See Otsuka Pharm. Co., Ltd. v. Apotex Corp., ___ F. Supp. 3d ____, 2015 WL 5720552 (D.N.J. Sept. 25, 2015).

[2] Defendants initially requested time to argue the phrase "aripiprazole drug substance" during the Markman hearing. Nevertheless, by letter dated October 16, 2015, the majority of Defendants withdrew their request to present any argument on the term, and instead rested upon their papers. [See, e.g., Docket Item 160 in Civil Action No. 14-1078.]

at 2 (arguing that claim construction proves overall unnecessary, because the disputed phrases have "readily ascertainable and understandable" plain and ordinary meanings).) Defendants argue, by contrast, that the intrinsic record provides a specific definition for each of the disputed phrases, and/or demonstrates that the various claim phrases prove incapable of construction on indefiniteness grounds.[3] (See, e.g., Defs.' Opening Claim Constr. Br. at 2-3.)

The Court has had the benefit of extensive briefing, argument and testimony at an all-day Markman hearing.[4] For the reasons that follow, the Court construes the disputed phrases as follows:[5]

---

[3] Actavis staked out and briefed claims construction positions on "Anhydrous Aripiprazole Crystals B" and "aripiprazole drug substance" separately from the remaining generic Defendants. (See generally Actavis's Opening Claim Constr. Br.) Nevertheless, because Otsuka voluntarily dismissed its claims against Actavis on November 10, 2015, the Court need not reach the merits of Actavis's claims construction positions.

[4] The Court conducted a Markman hearing on October 19, 2015, at which time the Court received a technical tutorial from Otsuka's experts, Stephen R. Byrn, Ph.D (hereinafter, "Dr. Byrn") and Christoph U. Correll, M.D. (hereinafter, "Dr. Correll"), as well as Defendants' experts, Dr. Graham Buckton, Robin D. Rogers, Ph.D (hereinafter, "Dr. Rogers"). In addition, the parties conducted limited cross-examination (and redirect) of Defendants' experts, Dr. Buckton, Dr. Rogers, and Ira S. Halper, M.D. (hereinafter, "Dr. Halper").

[5] The record amassed by the parties in connection with the pending Markman submissions spans thousands of pages and includes lengthy declarations from Otsuka's two experts, Dr. Byrn and Dr. Correll, and Defendants' four experts, Dr. Graham Buckton, Dr. Rogers, Anthony Palmieri III, Ph.D, R.Ph (hereinafter, "Dr. Palmieri"), and Dr. Halper. Defendants

Term	Court's Construction
"Anhydrous Aripiprazole Crystals B"	Anhydrous aripiprazole Crystalline substance, having: 1) a proton nuclear magnetic resonance spectrum (DMSO-d6, TMS) having characteristic peaks at [specified levels]; 2) a powder x-ray diffraction spectrum having characteristic peaks at [specified levels]; 3) clear infrared absorption bands at [specified levels] on the IR (KBr) spectrum; [] 4) an endothermic peak near about 141.5° C. in thermogravimetric/ differential thermal analysis (heating rate 5 ° C./min); 5) an endothermic peak near about 140.7° C. in differential scanning calorimetry (heating rate 5° C./min); and 6) low hygroscopicity, all as specifically defined in the specification of the '615 patent at 9:37-63 [or the '796 patent at 9:34-60]
"mean particle size"	*INDEFINITE*
"wherein said low hygroscopicity is defined as a moisture content of [0.40%/0.10%] or less after placing said substance/Crystals for 24 hours in a desiccator maintained at a temperature of 60° C and a humidity level of	wherein said low hygroscopicity is defined as a moisture content of 0.40% or less [0.10% or less] after the "Hygroscopicity-Test Method" in the specification of the '615 patent at 22:56-64 [or the '796 patent at 22:59-67; or the '760

initially also relied upon Robert J. Orr, Ph.D (hereinafter, "Dr. Orr") in support of their construction positions relative to the phrase "aripiprazole drug substance." Nevertheless, by letter dated October 16, 2015, Defendants withdrew their reliance upon Dr. Orr's opening and responsive declarations (and opted, as stated above, to rest upon their written submissions on this term). [See, e.g., Docket Item 160 in Civil Action No. 14-1078.] As a result, Dr. Orr did not appear at the Markman hearing, and the Court disregards, as it must, any arguments that rested upon his opinions.

100%”	**patent at 22:56-64].**
“aripiprazole drug substance”	**a drug substance that consists of aripiprazole, either in pure chemical form or as the active chemical ingredient in finalized form**
“a/the pharmaceutical composition” / “in combination with”	**a single dosage form, or “pharmaceutical composition,” containing at least two active ingredients aripiprazole and at least one of citalopram, escitalopram and salt thereof**

II. BACKGROUND

A. Factual and Procedural Background[6]

As this Court has summarized previously, Otsuka holds New Drug Application (hereinafter, “NDA”) No. 21-436, approved by the Food and Drug Administration (hereinafter, the “FDA”), for aripiprazole tablets, which Otsuka markets for the treatment of certain psychiatric conditions under the trade name Abilify®. In connection with Abilify’s® listing in the Orange Book, the FDA’s book of drug products approved under the Food, Drug, and Cosmetic Act (hereinafter, the “Orange Book”), 21 U.S.C. § 355(j), Otsuka identifies, in relevant part, the ’615, the ’796, the ’760, and the ’350 Patents.[7]

[6] For purposes of the pending Markman submissions, the Court need not retrace the detailed factual and procedural history of these complex infringement actions, and writes primarily for the parties.

[7] Otsuka’s Orange Book listing also identifies the ’528 Patent, the primary aripiprazole compound patent, as well the ’600 Patent, which claims certain methods of treatment in connection with the administration of aripiprazole.

1. Aripiprazole, Generally

Aripiprazole, an older compound with a complex molecular structure, acts as an atypical antipsychotic agent useful for the treatment of schizophrenia, among other central nervous system disorders. (See, e.g., Markman Hr'g Tr. at 21:19-22:2, 39:8-12.)

2. The '615, '796, and '760 Patents: Otsuka's Aripiprazole Polymorph Patents

The '615, the '796, and the '760 Patents issued on separate dates,[8] but all disclose a "Low Hygroscopic Aripiprazole Drug Substance and Processes for the Preparation Thereof."[9] (See, e.g., '615 Patent at 1:45-52.) In simple terms, these patents claim novel forms of anhydrous aripiprazole that have low hygroscopicity.

Prior art anhydrous aripiprazole forms proved "significantly hygroscopic," meaning that the forms would readily take on water and convert to a hydrous form if exposed to moisture. (Id. at 1:50-57.) As a result, these prior art forms suffered from less bioavailability and dissolubility, batch-to-batch variability, and a "significantly decreased"

[8] The '615 Patent issued on September 13, 2011, the '796 Patent issued on November 12, 2013, and the '760 Patent issued on February 4, 2014.

[9] As acknowledged by the parties, the '615, '796, and '760 Patents share a common specification, and for that reason, the Court only cites to one illustrative specification, unless otherwise indicated.

shelf-life. (Id. at 1:58-2:13; see also Markman Hr'g Tr. at 33:13-24; 60:22-61:12.)

The novel forms disclosed by the '615, the '796, and the '760 Patents claim to have solved these problems, particularly the susceptibility to moisture that plagued prior art anhydrous aripiprazole forms. (See, e.g., '615 Patent at 1:45-52.) The anhydrous aripiprazole forms disclosed by these patents specifically consist of "novel anhydrous aripiprazole crystals" that have "reduced hygroscopicity,"[10] rendering them more amenable than prior art formulations to "pharmaceutical processing and formulation," and enhancing their overall shelf-life, dissolubility, and bioavailability. ('615 Patent at 2:29-52; see also Markman Hr'g Tr. at 33:7-34:4.) In other words, these aripiprazole crystals have a decreased tendency to take on water, thereby enhancing the claimed aripiprazole tablets overall efficacy for the treatment of various mood disorders. (See generally Markman Hr'g Tr. at 33:7-34:4.)

The asserted claims of the '615, the '796, and the '760 Patents, in turn, teach the process for preparing the low hygroscopic aripiprazole (the '615 Patent), as well as claiming

[10] As explained by Dr. Byrn and Dr. Rogers, hygroscopicity specifically refers to the tendency of a material to sorb water, and includes both adsorption (where the water molecules interact with, but do not penetrate the crystal surface) and absorption (where the water molecules actually penetrate into the crystals). (See, e.g., Markman Hr'g Tr. at 24:11-13, 39:15-21.)

two of its forms: one in a pure crystal form (the ’796 Patent) and the other in a finalized form (the ’760 Patent). Independent claims 3 and 4 of the ’615 Patent, for example, disclose:[11]

> 3. and 4. A pharmaceutical solid oral preparation comprising Anhydrous Aripiprazole Crystals B having low hygroscopicity and one or more pharmaceutically acceptable carriers, wherein said low hygroscopicity is a moisture content of [0.40%/0.10%] or less after placing said Crystals for 24 hours in a desiccator maintained at a temperature of 60°C and a humidity level of 100%;
>
> wherein said crystals
>
> have a powder x-ray diffraction spectrum having characteristic peaks at 2Θ=11.0°, 16.6°, 19.3°, 20.3°, and 22.1°;
>
> have particular infrared absorption bands at 2945, 2812, 1678, 1627, 1448, 1377, 1173, 960, and 779 cm-1 on the IR (KBr) spectrum;
>
> exhibit an endothermic peak near about 141.5°C in thermogravimetric/differential thermal analysis (heating rate 5° C/min);
>
> exhibit an endothermic peak near about 140.7°C in differential scanning calorimetry (heating rate 5°C/min); and
>
> have a mean particle size of 50 μm or less, wherein said pharmaceutical solid oral preparation has at least one dissolution rate selected from the group consisting 60% or more at pH 4.5 after 30 minutes, 70% or more at pH 4.5 after 60 minutes, and 55% or more at pH 5.0 after 60 minutes.

(’615 Patent at 44:40-45:22.) The ’796 and ’760 Patents, each of which contain only two claims, then identify a specific low hygroscopic form of “anhydrous aripiprazole crystals B” and an

[11] Claims 3 and 4 of the ’615 Patent differ only in specific moisture content, with claim 3 teaching 0.40% or less, while claim 4 teaches 0.10% or less. (Compare ’615 Patent at 44:43-46 (claim 3), with ’615 Patent at 45:1-4 (claim 4).)

"aripiprazole drug substance," both of which have a moisture content below either 0.40% or 0.10% even after being placed in a desiccator maintained at a temperature of 60° C and a humidity level of 100%. (See '796 Patent at 44:23-32; '760 Patent at 44:23-32.) Simply put, these forms do not take on water, despite exposure to a high-moisture environment.

3. The '350 Patent: Otsuka's Asserted Method of Use Patent

The '350 Patent, by contrast, generally relates to a method of treating major depressive disorders through the adjunctive use of aripiprazole in conjunction with certain serotonin reuptake inhibitors (hereinafter, "SRIs"), and specifically discloses a "Carbostyril Derivatives and Serotonin Reuptake Inhibitors for Treatment of Mood Disorders."[12] The Patent describes, on its face, "pharmaceutical compositions" consisting of "carbostyril derivatives ... in combination with serotonin reuptake inhibitors in a pharmaceutically acceptable carrier" for the treatment of "mood disorders such as depression and major depressive disorder." ('350 Patent at 1:18-24.)

Independent claims 1-3, in turn, teach: a pharmaceutical composition comprising aripiprazole in combination with at least one serotonin reuptake inhibitor selected from citalopram, escitalopram and salts thereof. (See '350 Patent at 28:64-

[12] The '350 Patent issued on June 24, 2014, and therefore serves as the most recent of Otsuka's asserted follow-on patents.

29:6.) The remaining independent claims 9-11 then describe methods of treating specific mood disorders by administering an "effective amount" of the combination "pharmaceutical composition" disclosed in claims 1-3.[13] (Id. at 29:26-30:20.)

4. Otsuka's Infringement Litigation in this District

Beginning in early January 2014, the generic Defendants involved in these related infringement actions began to file ANDAs with the FDA, seeking approval to market generic aripiprazole tablets and/or orally disintegrating aripiprazole tablets,[14] prior to the expiration of the '615, '796, '760, '350

[13] The remaining claims of the '350 Patent, namely claims 4 through 8 and 12 through 18, all depend upon independent claims 1 through 3 and 9 through 11.

[14] Otsuka filed the first infringement action in this large series of actions on February 18, 2014, see Otsuka Pharm. Co., Ltd. v. Torrent Pharm., Inc., Civil Action No. 14-1078 (JBS/KMW), followed shortly thereafter by a cascade of thirty related actions: Otsuka Pharm. Co., Ltd. v. Alembic Global Holding SA, Civil Action No. 14-2982 (JBS/KMW) (filed May 9, 2014); Otsuka Pharm. Co., Ltd. v. Zydus Pham. USA Inc., Civil Action No. 14-3168 (JBS/KMW) (filed May 16, 2014); Otsuka Pharm. Co., Ltd. v. Aurobindo Pharma Ltd., Civil Action No. 14-3306 (JBS/KMW) (filed May 23, 2014); Otsuka Pharm. Co., Ltd. v. Intas Pharm. Ltd., Civil Action No. 14-3996 (JBS/KMW) (filed June 20, 2014); Otsuka Pharm. Co., Ltd. v. Zydus Pham. USA Inc., Civil Action No. 14-3168 (JBS/KMW) (filed May 16, 2014); Otsuka Pharm. Co., Ltd. v. Sun Pharm. Indus., Ltd., Civil Action No. 14-4307 (JBS/KMW) (filed July 7, 2014); Otsuka Pharm. Co., Ltd. v. Mylan Inc., Civil Action No. 14-4508 (JBS/KMW) (filed July 11, 2014); Otsuka Pharm. Co., Ltd. v. Torrent Pharm., Inc., Civil Action No. 14-4671 (JBS/KMW) (filed July 25, 2014); Otsuka Pharm. Co., Ltd. v. Zhejiang Huahai Pharm. Co., Civil Action No. 14-5537 (JBS/KMW) (filed September 4, 2014); Otsuka Pharm. Co., Ltd. v. Ajanta Pharm. Ltd., Civil Action No. 14-5876 (JBS/KMW) (filed September 19, 2014); Otsuka Pharm. Co., Ltd. v. Teva Pharm. USA, Inc., Civil Action No. 14-5878 (JBS/KMW) (filed September 19, 2014); Otsuka Pharm. Co., Ltd. v. Intas Pharm. Ltd., Civil Action No. 14-6158 (JBS/KMW) (filed October 2, 2014); Otsuka Pharm. Co., Ltd. v. Sun Pharm. Indus., Ltd., Civil Action No. 14-6397 (JBS/KMW) (filed October 6, 2014); Otsuka Pharm. Co., Ltd. v. Teva Pharm. USA, Inc., Civil Action No. 14-6398 (JBS/KMW) (filed September 19, 2014) (filed October 10, 2014); Otsuka Pharm. Co., Ltd. v. Aurobindo Pharma Ltd., Civil Action No. 14-6890 (JBS/KMW) (filed October 31, 2014); Otsuka Pharm. Co., Ltd. v. Lupin Ltd., Civil Action No. 14-7105 (JBS/KMW) (filed November 3, 2014); Otsuka Pharm. Co., Ltd. v. Actavis Elizabeth LLC, Civil Action No. 14-7106 (JBS/KMW) (filed November 10,

Patents.[15] Each Defendants' ANDA, however, included a "paragraph iv" certification, advancing their positions that their ANDAs would not infringe any of the valid patents-in-suit, and/or a "section viii" statement, certifying that the applicant would not seek approval for any indications or uses asserted to be covered by the '350 Patent. See Otsuka, ___ F. Supp. 3d ____, 2015 WL 1782653, at *5, *15. In other words, each Defendant,

---

2014; voluntarily dismissed November 12, 2015); Otsuka Pharm. Co., Ltd. v. Zydus Pham. USA Inc., Civil Action No. 14-7252 (JBS/KMW) (filed November 20, 2014); Otsuka Pharm. Co., Ltd. v. Alembic Pharm., Ltd., Civil Action No. 14-7405 (JBS/KMW) (filed November 26, 2014); Otsuka Pharm. Co., Ltd. v. Apotex Corp., Civil Action No. 14-8074 (JBS/KMW) (filed December 24, 2015); Otsuka Pharm. Co., Ltd. v. Hetero Drugs, Ltd., Civil Action No. 15-161 (JBS/KMW) (filed January 8, 2015); Otsuka Pharm. Co., Ltd. v. Amneal Pharm. Co, Ltd., Civil Action No. 15-1585 (JBS/KMW) (filed March 2, 2015); Otsuka Pharm. Co., Ltd. v. Sandoz Inc., Civil Action No. 15-1716 (JBS/KMW) (filed March 9, 2015; voluntarily dismissed on November 4, 2015); Otsuka Pharm. Co., Ltd. v. Indoco Remedies Ltd., Civil Action No. 15-1967 (JBS/KMW) (filed March 17, 2015; stayed and administratively terminated on September 15, 2015); Otsuka Pharm. Co., Ltd. v. Macleods Pharms. Ltd., Civil Action No. 15-5109 (JBS/KMW) (filed July 2, 2015); Otsuka Pharm. Co., Ltd. v. Standard Chem. & Pharm. Co., Civil Action No. 15-6353 (JBS/KMW) (filed August 21, 2015); Otsuka Pham Co., Ltd. v. Aurobindo Pharma Ltd., Civil Action No. 15-7584 (JBS/KMW) (filed October 19, 2015); Otsuka Pham Co., Ltd. v. Zydus Pharm. USA Inc., Civil Action No. 15-7802 (JBS/KMW) (filed October 30, 2015); and Otsuka Pharm Co., Ltd. v. Amneal Pharm. LLC, Civil Action No. 15-7803 (JBS/KMW) (filed October 30, 2015). Three of the more recent and less advanced cases, Indoco, Macleods, and Standard Chem., are not part of the pending Markman Defendants.

[15] As the lengthy exclusivity period of the patent covering the primary aripiprazole compound came to a close, Otsuka moved to enjoin the defendants from launching competing generic aripiprazole products, on the grounds that the package inserts or labels for the proposed generic products in all of the related infringement actions would induce infringement of claim 1 of the '350 Patent. See generally Otsuka Pharm. Co., Ltd., ___ F. Supp. 3d ____, 2015 WL 1782653, at *3–*4 (hereinafter, the "TRO Opinion"). Otsuka moved to amend its Complaints in order to assert the '350 Patent, for the first time, against Zydus, Torrent, and Teva. See id. On April 16, 2015, the Court granted Otsuka's motions to amend, principally in light of the liberal standard for amendment under Federal Rule of Civil Procedure 15(a). See id. at *4–*6; see also Otsuka Pharm. Co. v. Zydus Pharm. USA, No. 14-3168, 2015 WL 5950091, at *1 (D.N.J. Oct. 13, 2015).

and indeed all generic defendants in these related infringement actions, purport to seek approval for a noninfringing aripiprazole product. See generally id.

Otsuka filed infringement actions in this District, alleging that these Defendants proposed generic aripiprazole products will infringe at least one claim of the '615, '796, '760, and/or the '350 patents, among the other patents covering Otsuka's Abilify® product.[16]

III. CLAIM CONSTRUCTION STANDARD[17]

Claim construction focuses upon the intrinsic evidence, "including the claims themselves, the specification, and the prosecution history of the patent."[18] Sunovion Pharm., Inc. v. Teva Pharm. USA, Inc., 731 F.3d 1271, 1276 (Fed. Cir. 2013)

---

[16] Otsuka has, in some instances, asserted different combinations of the patents-in-suit against a particular generic Defendant, based upon the nature of its proposed ANDA product. The slight differences in the patents asserted in each action, however, have no impact on the pending issue of claims construction.

[17] The construction of claim terms constitutes a question of law, Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1995), aff'd, 517 U.S. 370 (1996), and the Court need not follow the parties' proposed constructions. See Marine Polymer Techs., Inc. v. HemCon, Inc., 672 F.3d 1350, 1359 n.4 (Fed. Cir. 2012) (en banc).

[18] If, however, the intrinsic evidence fails to disclose the meaning of a term, the Court may examine extrinsic evidence to determine the meaning of particular terminology to those of skill in the art of the invention. Phillips, 415 F.3d at 1318. The Court of Appeals for the Federal Circuit, however, cautions against "heavy reliance" upon extrinsic sources divorced from the intrinsic evidence because it "risks transforming the meaning of the claim term to the artisan into the meaning of the term in the abstract," and out of the context of the specification. Id. at 1321.

(citing Phillips v. AWH Corp., 415 F.3d 1303, 1315–17 (Fed. Cir. 2005) (en banc); Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Claim terms must, however, ordinarily be "given their plain and ordinary meanings to one of skill in the art" at the time of the invention "when read in the context of the specification and prosecution history." Golden Bridge Tech., Inc. v. Apple Inc., 758 F.3d 1362, 1365 (Fed. Cir. 2014) (citing Phillips, 415 F.3d at 1315–17). Nevertheless, the Court of Appeals for the Federal Circuit has routinely stated 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.'" Shire Dev., LLC v. Watson Pharms., Inc., 746 F.3d 1326, 1330 (Fed. Cir. 2014) (quoting Phillips, 415 F.3d at 1316).

IV. DISCUSSION

The parties, as stated above, request construction of the following five phrases: (1) "Anhydrous Aripiprazole Crystals B," (2) "mean particle size," (3) "wherein said low hygroscopicity is defined as a moisture content of [0.40%/0.10%] or less after placing said substance/Crystals for 24 hours in a desiccator maintained at a temperature of 60° C and a humidity level of 100%," (4) "aripiprazole drug substance," and (5) "a/the pharmaceutical composition" / "in combination with." The Court will address each claim phrase in turn.

A. "Anhydrous Aripiprazole Crystals B"[19]

The '615, '796, and '760 Patents aim, as stated above, to provide "novel anhydrous aripiprazole crystals," and specifically to disclose the inventors' discovery of a reduced-hygroscopic crystalline form of aripiprazole, "Anhydrous Aripiprazole Crystals B."[20] (See, e.g., '796 Patent at 2:47-48.)

In terms of defining "Anhydrous Aripiprazole Crystals B," the parties advance the following competing constructions:

Otsuka's Proposed Construction	Defendants' Proposed Construction
The phrase "Anhydrous Aripiprazole Crystals B" according to its plain and ordinary meaning means Anhydrous Aripiprazole Crystals B identifiable by reference to one or more of the features described in, for example, the '615 patent at col. 9:37-61 [or the '796 patent at col. 9:34-58].[21]	Anhydrous aripiprazole crystalline substance having the 1H-NMR spectrum, powder x-ray diffraction spectrum, infrared absorption bands, endothermic peak in thermogravimetric/ differential thermal analysis, endothermic peak in differential scanning calorimetry, and low hygroscopicity, as defined in the specification of the '615 patent at 9:37-63 [or the '796 patent at 9:34-60].

[19] As stated above, this disputed phrase appears in asserted claims 3, 4, 15, and 16 of the '615 Patent, claims 1 and 2 of the '796 Patent, and claims 4 and 12 of the '350 Patent

[20] The '615, '796, and '760 Patents also disclose "Anhydrous Aripiprazole Crystals C to G." (See, e.g., '615 Patent at 11:3-18:53.) The asserted claims of the '615, '796, and '760 Patents do not, however, recite these alternative crystalline forms.

[21] The Court finds Otsuka's proposed construction fatally flawed, at the outset, to the extent it attempts to construe the phrase by reference to the exact phrase requiring construction. Such a proposal amounts, at least in part, to no proposed construction at all. Moreover, Otsuka's reliance upon a "plain and ordinary meaning" is belied by the fact that these patents purport to disclose, for the first time, the novel crystalline form "Anhydrous Aripiprazole Crystals B." This highly technical term has no plain and ordinary meaning, nor has Otsuka convincingly advanced one.

In other words, Otsuka argues that the specifications should be read in the disjunctive—requiring that the crystalline form of aripiprazole be identified by reference to one or more, but not all, of the analytical tests identified in the specification. (See generally Otsuka's Opening Claim Constr. Br. at 7-14.) In support of this position, Otsuka, armed with the opinion of its expert, submits that a person of ordinary skill would, in reviewing the Patents, use "judgment and scientific reasoning" to select the "one or two" appropriate techniques to characterize the aripiprazole crystals, rather than resorting to the full panoply of characterization methods. (Otsuka's Opening Claim Constr. Br. at 7-14; Otsuka's Responsive Claim Constr. Br. at 3-11.) Even more, Otsuka claims that defining the term "Anhydrous Aripiprazole Crystals B" by reference to all analytical techniques would contravene the "cardinal rule" of claim construction, by importing a limitation from the specifications into the claims. (Markman Hr'g Tr. at 62:24-63:7, 118:9-119:23.) As a result, Otsuka submits that "Anhydrous Aripiprazole Crystals B" should be construed as an aripiprazole form marked by "low hygroscopicity," and identified by one or more of the characterization techniques provided in the specification. (Id. at 119:16-132:12.)

Defendants, by contrast, take the position that the specification must be read in the conjunctive, requiring that

all of the enumerated characteristics be present in order to identify the claimed aripiprazole crystal form. (Defs.' Opening Claim Constr. Br. at 4-10; Defs.' Responsive Claim Constr. Br. at 3-11.) In support of this construction, Defendants, supported by their own experts, submit that the specification contains an express definition of the novel "Anhydrous Aripiprazole Crystals B," and therefore contend that their proposed construction rightly incorporates the specification in its entirety.[22] (See Markman Hr'g Tr. at 158:21-179:20.)

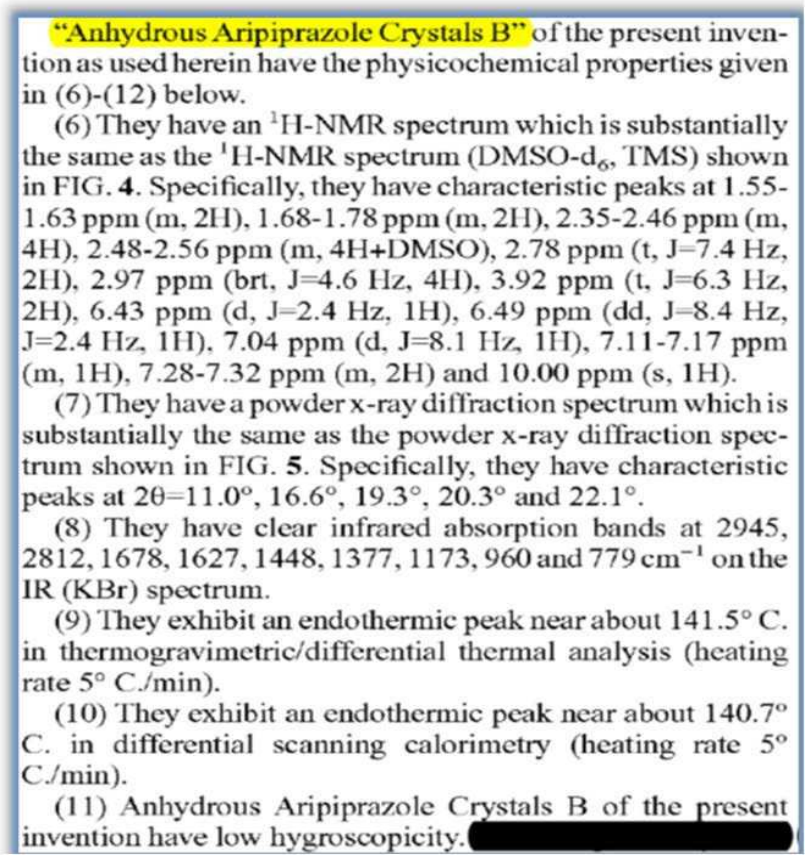
The Court begins by noting that the parties and their experts all acknowledge that a person of ordinary skill in the art would ordinarily identify a polymorph form through one or more of the illustrative characterization techniques identified in the specifications, namely, proton nuclear magnetic resonance spectroscopy (hereinafter, "NMR"), x-ray powder diffraction (hereinafter, "XRPD"), infrared spectroscopy (hereinafter, "IR"), thermogravimetric/differential thermal analysis (hereinafter, "TGA/DTA"), differential scanning calorimetry

[22] Otsuka quibbles with Defendants' construction on the ground that the construction, in essence, editorializes the specification by referencing the analytical tests by name only, and omitting the specific metrics recited in the specification. (See Markman Hr'g Tr. at 124:12-125:3.) Otsuka's argument, however, ignores the fact that Defendants' proposed construction plainly incorporates the specification in its entirety by reference. (See, e.g., Defs.' Opening Claim Constr. Br. at 4.) For that reason, the Court finds this narrow challenge without merit.

(hereinafter, "DSC"), and hygroscopicity testing. (See, e.g., Markman Hr'g Tr. at 31:4-16 (testimony of Otsuka's expert, Dr. Byrn, concerning his practice of selecting "one or two of the best methods"); 84:8-85:16 (testimony of Defendants' expert, Dr. Buckton, concerning his view that a scientist would "look at a raft of techniques for a particular material and depending [up]on the complexity ... would [then] decide which would be the appropriate techniques for that material"), 90:2-8 (testimony of Dr. Buckton concerning the ability to identify polymorphs without reference to the "large suite of techniques"); see also Byrn Dec. at ¶¶ 41-46.) Indeed, the parties' experts and their own submissions plainly reflect the industry practice of selecting the one or two most appropriate characterization methods based upon the nature of the tested material. (See, e.g., id. at 57:20-58:12.)

Nevertheless, the parties and their experts equally recognize that each analytical technique produces slightly different information relative to the identification of the polymorphic form (see, e.g., id. at 23:11-13, 31:12-16, 57:20-58:12), and consistently assert that the appropriate construction of the phrase "Anhydrous Aripiprazole Crystals B"

flows directly from some portion of the following language in the specifications:[23]



"Anhydrous Aripiprazole Crystals B" of the present invention as used herein have the physicochemical properties given in (6)-(12) below.

(6) They have an ^{1}H-NMR spectrum which is substantially the same as the ^{1}H-NMR spectrum (DMSO-d_6, TMS) shown in FIG. **4**. Specifically, they have characteristic peaks at 1.55-1.63 ppm (m, 2H), 1.68-1.78 ppm (m, 2H), 2.35-2.46 ppm (m, 4H), 2.48-2.56 ppm (m, 4H+DMSO), 2.78 ppm (t, J=7.4 Hz, 2H), 2.97 ppm (brt, J=4.6 Hz, 4H), 3.92 ppm (t, J=6.3 Hz, 2H), 6.43 ppm (d, J=2.4 Hz, 1H), 6.49 ppm (dd, J=8.4 Hz, J=2.4 Hz, 1H), 7.04 ppm (d, J=8.1 Hz, 1H), 7.11-7.17 ppm (m, 1H), 7.28-7.32 ppm (m, 2H) and 10.00 ppm (s, 1H).

(7) They have a powder x-ray diffraction spectrum which is substantially the same as the powder x-ray diffraction spectrum shown in FIG. **5**. Specifically, they have characteristic peaks at 2θ=11.0°, 16.6°, 19.3°, 20.3° and 22.1°.

(8) They have clear infrared absorption bands at 2945, 2812, 1678, 1627, 1448, 1377, 1173, 960 and 779 cm^{-1} on the IR (KBr) spectrum.

(9) They exhibit an endothermic peak near about 141.5° C. in thermogravimetric/differential thermal analysis (heating rate 5° C./min).

(10) They exhibit an endothermic peak near about 140.7° C. in differential scanning calorimetry (heating rate 5° C./min).

(11) Anhydrous Aripiprazole Crystals B of the present invention have low hygroscopicity. [redacted]

(See '615 Patent at 9:36-63; '760 Patent at 9:37-63; '796 Patent at 9:34-60.)

[23] Although "Anhydrous Aripiprazole Crystals B" appears in asserted claims 3, 4, 15 and 16 of the '615 Patent, claims 1 and 2 of the '796 Patent, and claims 4 and 12 of the '350 Patent, no party argues that the claims language itself provides a basis from which to divine the meaning of the disputed term. For that reason, the Court turns, as it must, to the specifications. See Phillips, 415 F.3d at 1315 (citations omitted) (reaffirming the "long emphasized" and often "'dispositive'" importance of the specification in claim construction); see also Safety Rail Source, LLC v. Bilco Co., 656 F. Supp. 2d 468, 475 (D.N.J. 2009) (citation omitted) ("the Court must consult the specification in order to determine whether it 'expressly defines terms used in the claims or ... [whether] it defines terms by implication'").

The ’615, ’796, and ’760 Patents each state, in their introductory sections, that their disclosures define “Anhydrous Aripiprazole Crystals B” for purposes of the claimed inventions. (See ’615 Patent at 2:32-35 (noting that the ’615 Patent identifies a novel form of aripiprazole defined as “Anhydrous Aripiprazole Crystals B”); ’760 Patent at 2:31-34 (same); ’796 Patent at 2:28-31 (same).) The portion of the specifications relied upon by all parties then state, in clear language and under a heading bearing the title “Characterization of Anhydrous Aripiprazole Crystals B,” that the “‘Anhydrous Aripiprazole Crystals B’ of the present invention as used herein have the physicochemical properties given in (6)-(12) below.” (See ’615 Patent at 9:36-63; ’760 Patent at 9:37-63; ’796 Patent at 9:34-60.) Following that disclosure, the specifications delineate six, non-conditional physicochemical properties—or, in simpler terms, characterization techniques—in successively numbered paragraphs.

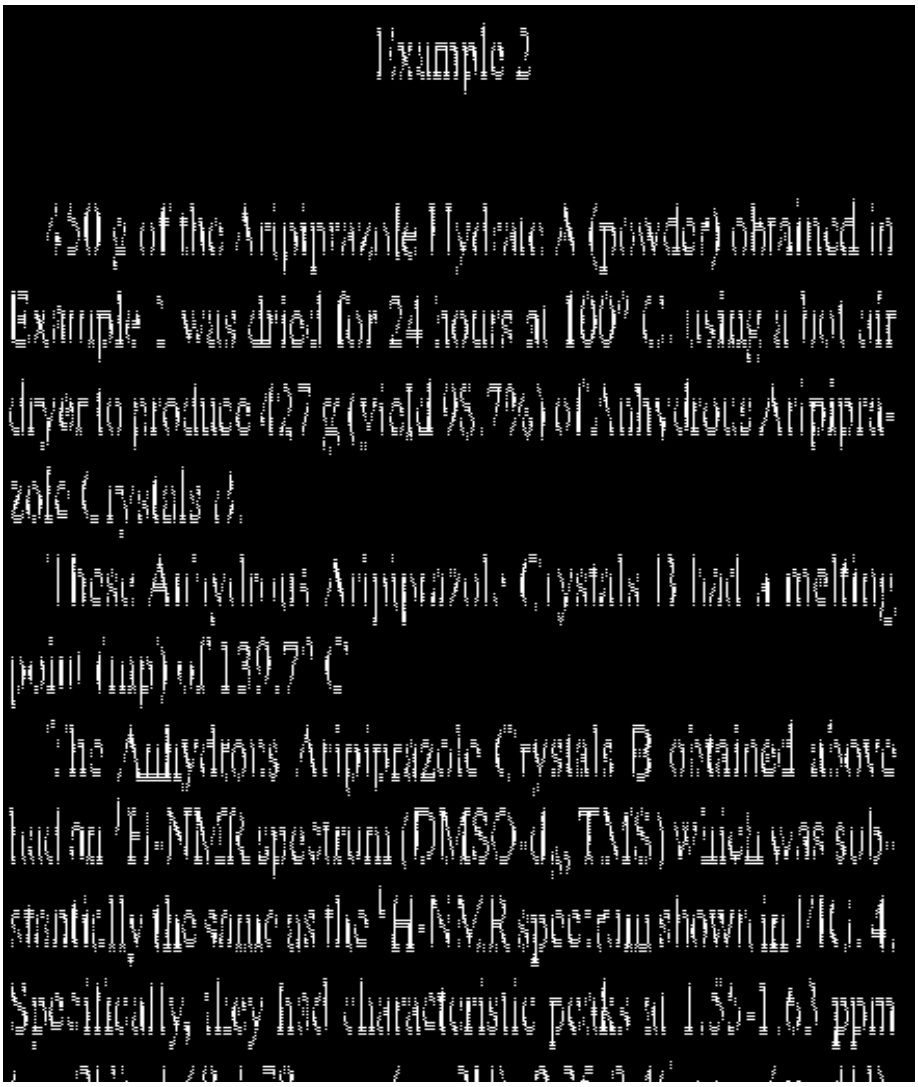
In that way, these portions of the specifications contain all of the features that signify a special definition of “Anhydrous Aripiprazole Crystals B” that requires all of the specified physicochemical properties (as advanced by Defendants), and not merely one or more (as claimed by Otsuka). See AstraZeneca LP v. Apotex, Inc., 633 F.3d 1042, 1051-52 (Fed. Cir. 2010) (discussing special definitions revealed by

specifications). Indeed, the mandatory language of the specifications, along with their structures, lead to the simple conclusion that the patentee intended to provide the phrase "Anhydrous Aripiprazole Crystals B" with a particular meaning for purposes of the '615, '796, and '760 Patents. Critically, the specifications not only set off the term "Anhydrous Aripiprazole Crystals B" with quotation marks—a strong indication, by itself, that the disclosures that follow constitute a definition—they also specifically state that the term has a particular meaning in the context of the patents-in-suit.[24] (See, e.g., '615 Patent at 9:37-38 ("'Anhydrous Aripiprazole Crystals B' of the present invention as used herein ...") (emphasis added); '760 Patent at 9:37-38 (same); '796 Patent at 9:37-38 (same).) See Abbott Labs. V. Andrx Pharms., Inc., 473 F.3d 1196, 1210-11 (Fed. Cir. 2007) (explaining that a patentee may expressly define certain claims' terms through the use of quotation marks and phrases like "as used herein").

[24] The Court finds Otsuka's reliance upon Aventis Pharms. Inc. v. Impax Labs, Inc., No. 02-1322, 2011 WL 94188, at *3 (D.N.J. Jan. 11, 2011) unconvincing. In Aventis, the court considered whether the following phrase "As used herein, the term 'suitable antiadherent' includes stearic acid, cetyl alcohol ... and the like" provided a special definition of "suitable antiadherent." Id. at *3. In rejecting quotation marks and the phrase "as used herein" as an indication of a definition, the Aventis court relied upon the fact that the accompanying sentence contained an array of nonexhaustive "examples" for the disputed term, rather than a clear definition. Id. at *3-*4. The disclosures relative to "Anhydrous Aripiprazole Crystals B," by contrast, contain strong definitional language.

Numbered paragraphs (6) through (12) then teach the specific contours of each analytical test, but provide no support for the flexible interpretation proposed by Otsuka. Nor any corresponding indication (like, for example, the inclusion of "or" between each numbered paragraph) that the characterization techniques should be viewed as interchangeable. Rather, these portions of the specification squarely reflect that the novel "Anhydrous Aripiprazole Crystals B" are those identified by each of the characterization techniques.

This construction then finds further support in the remainder of the specifications. The disclosures' examples, for instance, consistently describe "Anhydrous Aripiprazole Crystals B" by reference to all of the characterization methods. Indeed, Example 2 provides:



Example 2

450 g of the Aripiprazole Hydrate A (powder) obtained in Example 1 was dried for 24 hours at 100° C. using a hot air dryer to produce 427 g (yield 95.7%) of Anhydrous Aripiprazole Crystals B.

These Anhydrous Aripiprazole Crystals B had a melting point (mp) of 139.7° C.

The Anhydrous Aripiprazole Crystals B obtained above had an ^{1}H-NMR spectrum (DMSO-d_6, TMS) which was substantially the same as the ^{1}H-NMR spectrum shown in FIG. 4. Specifically, they had characteristic peaks at 1.55-1.63 ppm

(See, e.g., ’615 Patent at 26:2-37.) In other words, Example 2 describes “Anhydrous Aripiprazole Crystals B” based upon the results of all of the characterization techniques, namely, NMR, XRPD, IR, TGA/DTA, DSC, and hygroscopicity. (See, e.g., ’796 Patent at 26:1-28:15.) Dependent Examples 2 through 10 then consistently state that the “hygroscopic anhydrous aripiprazole crystals” obtained through various methods exhibited “the same ... physicochemical properties of the Anhydrous Aripiprazole

Crystals B." (See, e.g., '615 Patent at 26:39-28:16 (emphasis added).) This consistent usage lends itself to only one conclusion,[25] namely, that the patentee especially defined this term to require that the novel crystals be identified by each crystalline characterization technique.[26] See Metrologic Instruments, Inc. v. PSC Inc., No. 99-4876, 2003 WL 22077652, at *9 (D.N.J. Aug. 26, 2003) (citing Bell Atl. Network Serv., Inc. v. Covad Comm. Grp., 262 F.3d 1258, 1273 (Fed. Cir. 2001)).

[25] Otsuka's proposal of a construction that incorporates "one or more" of the "features" identified in the specifications, by contrast, finds no relevant support in the specification. (See Otsuka's Opening Claim Constr. Br. at 8; Otsuka's Responsive Claim Constr. Br. at 3.) Indeed, although the '615, '796, and the '760 Patents use the phrase "one or more" on 18 separate instances, none appear in relation to the properties of "Anhydrous Aripiprazole Crystals B." (See, e.g., '615 Patent at 5:58-61, 8:29-35, 12:54-67, 13:15-23, 13:29-33, and 13:43-51.) Even more critically, Otsuka's proposed construction claims that NMR would, by itself, prove sufficient to identify the claimed aripiprazole crystal, despite the fact that no party disputes that NMR identifies only the underlying compound (i.e., it identifies the presence of aripiprazole), and therefore cannot differentiate between various crystalline forms of aripiprazole. (See, e.g., Markman Hr'g Tr. at 24:3-9, 47:14-17, 57:23-25, 173:1-9; Byrn Opening Dec. at ¶ 50; Byrn Dep. Tr. at 117:7-10.)

[26] During the Markman hearing, counsel for Otsuka relied upon select figures and alternative embodiments, each of which rely upon only two analytical techniques. (See Markman Hr'g Tr. at 127:21-129:17; see also '615 Patent at 6:49-59, 7:9-18.) The Court of Appeals for the Federal Circuit, however, discourages constructions predicated upon figures and alternative embodiments, see Computer Docking Station Corp. v. Dell, Inc., 519 F.3d 1366, 1374 (Fed. Cir. 2008), and the embodiments cited by Otsuka refer only to an "aripiprazole drug substance," not "Anhydrous Aripiprazole Crystals B." For these reasons, the Court finds that these references have limited relevance to the construction of "Anhydrous Aripiprazole Crystals B."

Moreover, even in the absence of this consistent language, the Court finds creditable Defendants' position that Otsuka has, on numerous occasions, admitted that "Anhydrous Aripiprazole Crystals B" should be defined by reference to five analytical techniques, and not the "one or more" construction it advances here. Indeed, in prosecuting the European equivalent of the '615, '796, and the '760 Patents, EP1330249 (hereinafter, "EP1"), Otsuka repeatedly defined the "Aripiprazole anhydrous form B" disclosed in the EP1 in terms of its "XRD pattern, the IR spectrum, the endothermic peak in thermogravimetric/differential thermo analysis, the endothermic peak in DSC **and**, most importantly, the low hygroscopicity." (Ex. K to Second Buckton Dec. at 1 (emphasis in original); see also Second Buckton Dec. at ¶¶ 19-22.)

In other words, Otsuka insisted, in connection with an indisputably familial patent, that the five crystal characterization techniques—XRPD, IR, TGA/DTA, DSC, and low hygroscopicity—together, and not alone, defined "Anhydrous Aripiprazole Crystals B" from other crystal forms.[27] The EP1 has substantively similar claims, contains a similar specification,

[27] NMR does not, as stated above, identify crystalline forms. As a result, it comes as little surprise that asserted claims 3 and 4 of the '615 Patent identify the "Anhydrous Aripiprazole Crystals B" only by reference to XRPD, IR, TGA/DTA, DSC, and low hygroscopicity. Nevertheless, because it does not limit claim scope, the Court will include NMR in its construction of this disputed term.

and proves entirely consistent with the invention described by the specification of the '615, '796, and '760 Patents. Therefore, the Court finds that Otsuka's statements to the EPO lend even further support for the construction supported by the specification.[28] See Baxter Healthcare Corp. v. HQ Specialty Pharma Corp., ___ F. Supp. 3d ____, 2015 WL 5646779, at *9 (D.N.J. Sept. 23, 2015) (citing instructive cases, and holding the patentee to its clear statements before the EPO).

For all of these reasons, the Court finds that the specification explicitly teaches that the phrase should be construed by reference to all of the analytical tests,[29] and will

[28] As this Court recently explained, "[t]he Court of Appeals for the Federal Circuit 'cautions against indiscriminate reliance on the prosecution of corresponding foreign applications in the claim construction analysis,' particularly if the statements made during the foreign prosecution arose in response to unique aspects of foreign patent law." Baxter, ___ F. Supp. 3d ____, 2015 WL 5646779, at *9 (citations omitted). "Nevertheless, the Federal Circuit has routinely approved reliance upon statements in foreign prosecutions where they constituted 'blatant admissions' directed at the relevant art, and where the statements proved otherwise 'consistent with the claims and the invention described in the specification' at issue." Id. Application of these principles to this action provides ample support for holding Otsuka to its statements during the European prosecution. See id. (collecting relevant cases).

[29] The Court finds Otsuka's reliance upon Dr. Buckton's prior publications and the unrelated aripiprazole patents of Sandoz AG, Hetero Drugs Limited, and Teva Pharmaceutical Industries Ltd. unconvincing. (See Markman Hr'g Tr. at 129:24-132:12.) These extrinsic sources, consisting of non-familial patents and publications on unrelated compounds, provide further confirmation for the undisputed industry practice in characterizing crystal polymorphs, but do little to inform the special definition analysis in this instance. See Apple Inc. v.

adopt Defendants' proposed construction (in slightly modified form).[30] See In re Pabst Licensing Digital Camera Patent Litig., 778 F.3d 1255, 1261 (Fed. Cir. 2015) (explaining that district courts should adopt the construction that "stays true to the claim language and most naturally aligns with the patent's description of the invention").

B. "mean particle size"[31]

Asserted claim 3 of the '615 Patent generally discloses, in relevant part, low hygroscopic Anhydrous Aripiprazole Crystals B, wherein these Crystals "have a mean particle size of 50 μm or less..." ('615 Patent at 44:59 (emphasis added).) With respect to the phrase "mean particle size," the parties advance the following competing constructions:

Otsuka's Proposed Construction[32]	Defendants' Proposed Construction
The phrase "mean particle size" has its plain and ordinary meaning as	*Indefinite (i.e., the claim, even read in light of the specification and the*

Motorola, Inc., 757 F.3d 1286, 1312 (Fed. Cir. 2014) (stating that unrelated patents have no relevance to claim construction), reversed in part on other grounds, William v. Citrix Online, LLC, 792 F.3d 1339 (Fed. Cir. 2015) (en banc).

[30] Finally, because Otsuka asserts that the term "Anhydrous Aripiprazole Crystals B" should be construed similarly across the '615 and the '796 Patents, the Court finds no support for the position that Defendants' proposed construction improperly cross-incorporates limitations between these patents. Nor does the Court find that the narrower scope of claims 3 and 4 of the '615 Patent require adoption of Otsuka's construction. Rather, these claims further limit "Anhydrous Aripiprazole Crystals B" for purposes of claims 3 and 4, but do not otherwise restrict the meaning of the term in relation to the overall Patents.

[31] As stated above, this disputed phrase appears in asserted claims 3, 4, 15, and 16 of the '615 Patent.

[32] Otsuka's proposed construction has, as explained below, changed over time.

understood by a person of ordinary skill in the art[33] **-or-** "mean particle size" means to "analogous to mean equivalent spherical volume diameter by laser light diffraction scattering" **-or-** "mean particle size" refers to "volume mean particle size" **-or-** "mean particle size" means "volume weighted mean"	*prosecution history, fails to inform, with reasonable certainty, those skilled in the art concerning the scope of the invention)*

Otsuka argues, in particular, that the intrinsic record make "clear that a person of ordinary skill in the art would readily have understood that 'mean particle size' refers to volume mean particle size," particularly because the claims teach that "mean particle size" should be measured using a "laser diffraction particle size analyzer." (Otsuka's Responsive Claim Constr. Br. at 12 (citation omitted).) Defendants, by contrast, take the position that the term proves "indefinite" (or, incapable of construction), because it's amenable to multiple meanings. (Defs.' Opening Claim Constr. Br. at 12-15; Defs.' Responsive Claim Constr. Br. at 11-16.) Defendants specifically argue that the ordinary artisan would, in reviewing the disclosures, confront a number of unresolved

[33] Because all parties substantively agree that the phrase "mean particle size" has multiple meanings, the Court rejects at the outset Otsuka's position that the phrase has any "plain" meaning, and therefore requires no construction. (See, e.g., Otsuka's Opening Claim Constr. Br. at 18.)

issues that "directly affect the output of the particle size analysis," particularly given the array of possible interpretations for the terms "'means' and 'sizes.'"[34] (Defs.' Opening Claim Constr. Br. at 14-15.)

The parties' construction positions hinge upon issues of indefiniteness, an area of law that has undergone fundamental changes following Nautilus, Inc. v. Biosig Instruments, Inc., ___ U.S. ____, 134 S. Ct. 2120 (2014), which is next addressed.

1. Standard for Indefiniteness

"A patent must 'conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as [the] invention.'" Media Rights Techs., Inc. v. Capital One Fin. Corp., ___ F.3d ____, No. 2014-1218, 2015 WL 5166358, at *3 (Fed. Cir. Sept. 4, 2015) (citing 35 U.S.C. § 112). A claim fails to satisfy this statutory requirement and proves "invalid for indefiniteness if its language, when read in light of the specification and the prosecution history, 'fail[s] to inform, with reasonable certainty, those skilled in the art about the scope of the

[34] Defendants further claim that Otsuka's "many conflicting constructions," namely, "plain and ordinary meaning," "analogous to mean equivalent spherical volume diameter by laser light diffraction scattering," "volume mean particle size," and "volume weighted mean," prove indefiniteness. (See Markman Hr'g Tr. at 180:17-185:5.)

invention.'" [35] Media Rights Techs., Inc., ___ F.3d ____, 2015 WL 5166358, at *3 (quoting Nautilus, ___ U.S. ____, 134 S. Ct. at 2124).

A claim may, for example, prove indefinite if its language "might mean several different things" and the patent itself identifies "no informed and confident choice ... among the contending definitions." Nautilus, ___ U.S. ____, 135 S. Ct. at 2130 n.8. Stated differently, in order to overcome an indefiniteness challenge, "the patent and prosecution history must disclose a single known approach or establish that, where multiple known approaches exist, a person having ordinary skill in the art would know which approach to select."[36] Dow Chemical Co. v. Nova Chemicals Corp (Canada), ___ F.3d ____, 2015 WL 5060947, at *6 (Fed. Cir. Aug. 28, 2015) (citation omitted); see

[35] In articulating this standard, Nautilus fundamentally "changed the law of indefiniteness." Dow Chem. Co., ___ F.3d ____, 2015 WL 5060947, at *6.

[36] For that reason alone, the Court rejects Otsuka's position that "mean particle size" should be found definite, simply because "other courts have readily construed the term 'mean particle size.'" (Otsuka's Opening Claim Constr. Br. at 15 (citing Eli Lilly & Co. v. Teva Pharm. USA, Inc., No. 06-1017, 2008 WL 2410420, at *1 (S.D. Ind. June 11, 2008).) In reality, Otsuka cites to only one case that construed the term, prior to the Supreme Court's articulation of a new indefiniteness test under Nautilus, and where neither party actually advanced an indefiniteness argument. See Eli Lilly & Co., 2008 WL 2410420, at *4-*5. Beyond these clearly distinguishing features, the indefiniteness inquiry focuses upon whether the relevant patent record discloses a single meaning among multiple possibilities, not whether an unrelated patent contained such disclosures. See Nautilus, Inc., ___ U.S. ____, 134 S. Ct. at 2124 (describing the standard for indefiniteness).

also Teva Pharms. USA, Inc. v. Sandoz, Inc., 789 F.3d 1335 (Fed. Cir. 2015) (same). In conceptualizing this framework, the Court finds two recent Federal Circuit decisions—both of which concern the indefiniteness of measurements—instructive.

In Teva Pharmaceuticals USA, Inc. v. Sandoz, Inc., 789 F.3d 1335 (Fed. Cir. 2015), the Federal Circuit applied the legal standards set forth in Teva Pharmaceuticals USA, Inc. v. Sandoz, Inc., ___ U.S. ____, 135 S.Ct. 831 (2015) and Nautilus, Inc. v. Biosig Instruments, Inc., ___ U.S. ____, 134 S. Ct. 2120, 2124 (2014), in order to resolve the question of indefiniteness regarding a claim limitation of U.S. Patent No. 5,800,808 (the "'808 patent")—"molecular weight of about 5 to 9 kilodaltons." 789 F.3d at 1338. The Teva parties agreed that "molecular weight" could refer to peak average molecular weight (M_p), number average molecular weight (M_n), and weight average molecular weight (M_w), and that each of those measures required a different calculation and would typically yield "a different result for a given polymer sample." Id. at 1338. The '808 patent specification, however, did not expressly define "molecular weight," nor did it use the terms M_p, M_n, or M_w. Id. Even more, the prosecution history contained inconsistent statements, with the patentee stating in one instance that "molecular weight" referred to M_w, and in another than it meant M_p. Id. at 1345. As a result, the Teva court found the term indefinite, despite

testimony from the patentee's expert that someone skilled in the art could, despite any ambiguity, have determined the intended measure. Id. at 1338, 1341, 1344-45.

Most recently, in Dow Chemical Co. v. Nova Chemicals Corp. (Canada), ___ F.3d ____, 2015 WL 5060947 (Fed. Cir. Aug. 28, 2015), the Federal Circuit again applied the recent Supreme Court decisions (as well as its own decision in Teva) to resolve the question of indefiniteness regarding a claim limitation of U.S. Patent Nos. 5,847,054 (the "'053 Patent") and 6,111,023 (the "'023 Patent")—"a slope of strain hardening coefficient greater than or equal to 1.3." Id. at *2. Similar to Teva, the phrase "slope of strain hardening" proved testable by at least "four methods," each of which would "produce different results, i.e., a different slope." Id. at *9. The intrinsic records, however, provided no guidance about "which method should be used." Id. As a result, the Federal Circuit found the claim limitations indefinite, despite the testimony from the patentee's expert that one of ordinary skill, in reviewing the specification, would have known to select the method the expert himself developed. Id. at *10. Commenting further on its earlier decision in the Teva case, the Federal Circuit noted in Dow that particularly "where difference approaches to measurements are involved," id. at *6 (citing Teva, 789 F.3d at 1341, 1344-45), the post-Nautilus standard requires that "'[t]he

claims, when read in light of the specification and the prosecution history, must provide objective boundaries for those of skill in the art.'" Dow Chemical Co., 2015 WL 5060947, at *6 (quoting Interval Licensing LLC v. AOL, Inc., 766 F.3d 1364, 1371 (Fed. Cir. 2010) (citing Nautilus, 134 S. Ct. at 2130 & n.8))).

2. The '615 Patent fails to inform, with reasonable certainty, the meaning of the phrase "mean particle size"

In applying this standard here, the Court finds that the facts of Teva and Dow closely resemble the claim limitation at issue here—"mean particle size." Indeed, even a cursory inspection of the intrinsic record demonstrates that the '615 Patent fails to provide the required guidance.

Indeed, Otsuka readily acknowledges the susceptibility of "mean particle size" to multiple measurements, each of which could yield varied results. (See Otsuka's Opening Claim Constr. Br. at 16-17; Otsuka's Responsive Claim Constr. Br. at 12-18.) Nevertheless, Otsuka submits that the '615 Patent, when viewed through the eyes of the person of ordinary skill in the art, reveals that "mean particle size" refers to "volume mean particle size." (Otsuka's Opening Claim Constr. Br. at 16.) In support of this position, Otsuka points to a narrow portion of the specification that identifies a laser diffraction particle

size analyzer,[37] and then to asserted dependent claims 15 and 16, both of which contain the limitation that the "mean particle size [be] measured using a laser diffraction particle size analyzer." ('615 Patent at 48:1-6.) Otsuka then argues that an ordinary artisan would, based upon industry literature, understand the reference to "particle size analysis via laser diffraction methods" as an instruction to construe "mean particle size" as "volume mean particle size."[38] (Otsuka's Opening Claim Constr. Br. at 16.)

The Court notes that only the asserted dependent claims of the '615 Patent, claims 15 and 16, limit particle size measurement to the laser diffraction technique. (See id. at 44:40-45:22.) The specification, however, specifically refers to a laser diffraction particle analyzer, and for that reason, the Court will presume that the '615 Patent overall instructs that particle size be measured by such technique.

---

[37] The cited portion of the specification reads:

> (6) Particle Size Measurement
> 0.1g of the particles to be measured were suspended in a 20 ml n-hexane solution of 0.5 g soy lecithin, and particle size was measured using a size distribution meter (Microtrack HRA, Microtrack Co.).

('615 Patent at 22:51-55.)

[38] As referenced above, Otsuka's proposed construction of "mean particle size" has been a moving target, ranging from "plain and ordinary meaning" to "analogous to mean equivalent spherical volume diameter by laser light diffraction scattering" to "volume mean particle size" and finally to "volume weighted mean"

Nevertheless, it remains undisputed that the laser diffraction measurement technique generates two "mean" measures: a volume weighted mean and a surface area weighted mean. (See, e.g., Second Buckton Dec. at ¶¶ 30-34, 40-41; Byrn Dep. at 200-01; Markman Hr'g Tr. at 76:19-22.) Despite these alternate measures, the parties' experts appear to agree, at least superficially, that the volume weighted mean constitutes one of the more frequently used measures for particle size analysis. (See, e.g., Markman Hr'g Tr. at 77:9-12; Byrn Dec. at ¶ 58 (arguing that secondary sources reflect the understanding a person of ordinary skill in the art would have had at the time of filing that "mean particle size" refers to the volume mean particle size).) A closer inspection of their various submissions, however, reveals the lack of uniform understanding in the relevant scientific community.

Specifically, Otsuka's expert, Dr. Byrn, states in his declaration that "volume mean particle size" constitutes the default meaning of "mean particle size" to one of ordinary skill. (See Byrn Dec. at ¶¶ 55-58; but see Byrn Dep. at 200:5-209 (discussing d(0.5) or the median distribution).) In reviewing a typical laser diffraction results analysis report during his deposition, however, Dr. Byrn took the position that "mean particle size" refers to the median volume distribution, or d(0.5), not the "volume weighted mean" or the "surface

weighted mean," and that such approach comported with the ordinary understanding. (Byrn Dep. at 200:5-209) Defendants' expert, Dr. Buckton, then testified that the "median is the most frequently used" measurement for particle size analysis (Markman Hr'g Tr. at 77:9-12 (emphasis added)), but acknowledges that "the volume-weighted mean" serves as the "the most frequently" presented mean. (Buckton Dep. at 424:4-9; see also Second Buckton Dec. at ¶ 39 (stating that volume weighted mean "is the most frequently used mean value, in [his] experience").)

Even more, the '615 Patent makes no connection between "mean particle size" and volumetric measures (although it speaks in terms of volume in unrelated contexts), and therefore provides no information from which to divine, with reasonable certainty, the appropriate measure of the "mean" for purposes of the '615 Patent. (See generally '615 Patent at 19:38-40.)

Nor does the '615 Patent instruct on the manner in which to characterize the "size" of the particle (see generally '615 Patent at 22:51-55), which can be defined by reference to any one of the following measures:

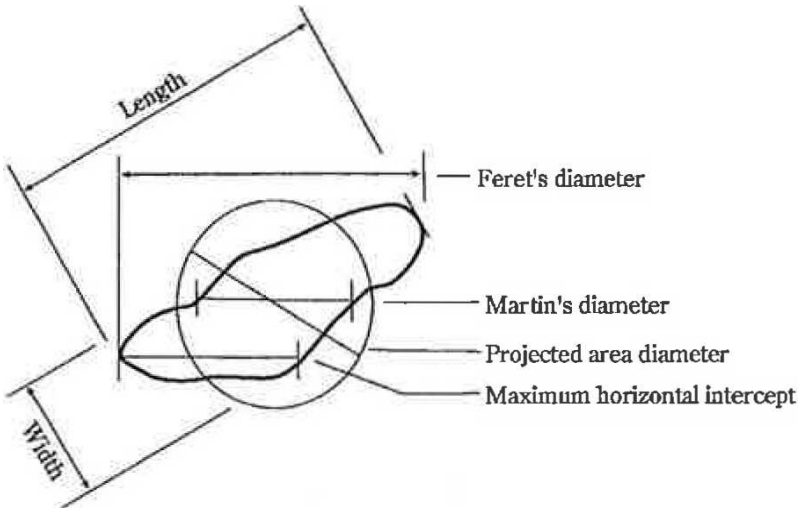


Fig. 3.04-1 Commonly used measurements of particle size

(Ex. S to Second Buckton Dec.)[39] In other words, a person of ordinary skill would be left to guess on how best to characterize particle size, among the array of possible descriptions.

In order to fill these gaps in the intrinsic record, Otsuka resorts entirely to the opinion of its own expert, Dr. Byrn. (See generally Byrn Dec. at ¶ 58; see also Otsuka's Responsive Claim Constr. Br. at 13 (arguing that "[n]one of Defendants' allegations prove Dr. Byrn wrong").) Nevertheless "a claim term is indefinite if it 'leave[s] the skilled artisan to consult the

[39] As explained by Dr. Buckton, the measurement of particle size varies in complexity based upon the shape of particle (spherical or irregular) and the number of measured particles. (See Second Buckton Dec. at ¶ 43.) Figure 3.04-1, in turn, depicts the "at least five types of optical microscopy" particle size determinations. (Second Buckton Dec. at ¶ 43 n.5.) These types specifically include length, width, Feret's diameter, Martin's diameter, and the maximum horizontal intercept. For that reason, particle size determination requires information on both the type of diameter measured and on the particle shape. The '615 Patent, however, provides no such disclosure.

'unpredictable vagaries of any one person's opinion,'" Dow Chem. Co., ___ F.3d ____, 2015 WL 5060947, at *10 (quoting Interval Licensing LLC v. AOL, Inc., 766 F.3d 1364, 1371 (Fed. Cir. 2014)), and Otsuka's reliance upon Dr. Byrn requires just that.

In this case, the wording of the claim term "mean" and specification may be construed as designating an instrument by which to conduct a measurement of "mean particle size," but nothing therein guides the skilled practitioner whether to utilize the "volume weighted mean" or the "surface weighted mean" that such a device reports as measurements. The choice of "volume" or "surface" matters because each type lends to a different result. Looking then to extrinsic evidence, Otsuka has not demonstrated that "volume weighted mean" is the default measurement that the ordinary skilled practitioner would select, given the clear absence of a convergence upon that convention in the field; this is the hallmark of an indefinite term. Similarly, as discussed above, the words "particle size" are likewise indefinite, as there are multiple accepted aspects of "size," each yielding a different result, and the intrinsic and extrinsic evidence does not narrow the field to the one aspect meant to establish the boundary of the invention, as discussed above.

For these reasons, the Court finds the term "mean particle size" indefinite. See Teva Pharms. USA, Inc., 789 F.3d at 1344-

45 (finding the term "molecular weight" indefinite); Dow Chemical Co., ___ F.3d ____, 2015 WL 5060947, at *10 (finding the claim term including the phrase "slope of strain" indefinite).

C. "wherein said low hygroscopicity is defined as a moisture content of [0.40%/0.10%] or less after placing said substance/Crystals for 24 hours in a desiccator maintained at a temperature of 60° C and a humidity level of 100%"[40]

Exemplar claims 3 and 4 of the '615 Patent disclose "A pharmaceutical solid oral preparation comprising Anhydrous Aripiprazole Crystals B having low hygroscopicity and one or more pharmaceutically acceptable carriers, wherein said low hygroscopicity is a moisture content of [0.40%/0.10%] or less after placing said Crystals for 24 hours in a desiccator maintained at a temperature of 60 º C and a humidity level of 100%..."[41] ('615 Patent at 44:40-45:22 (emphasis added).) With respect to the meaning of this phrase, the parties advance the following competing constructions:

[40] As stated above, this disputed phrase appears in asserted claims 3, 4, 15, and 16 of the '615 Patent, claims 1 and 2 of the '796 Patent, and claims 1 and 2 of the '760 Patent.

[41] The asserted claims of the '796 and the '760 Patents, in turn, claim Anhydrous Aripiprazole Crystals B and/or Aripiprazole drug substance "of low hygroscopicity wherein said low hygroscopicity is defined as a moisture content of [0.40%/0.10%] or less after placing said substance/Crystals for 24 hours in a desiccator maintained at a temperature of 60° C and a humidity level of 100%." ('796 Patent at 44:21-31; '760 Patent at 44:22–32.)

Otsuka's Proposed Construction	Defendants' Proposed Construction[42]	Teva's,[43] Prinston's, Zydus', Aurobindo's, and Amneal's Proposed Construction
The phrase "wherein said low hygroscopicity is defined as a moisture content of 0.4% or less [0.10% or less] after placing said drug substance/Crystals for 24 hours in a desiccator maintained at a temperature of 60° C and a humidity level of 100%" has its plain and ordinary meaning as understood by a person of ordinary skill in the art.	wherein said low hygroscopicity is defined as a moisture content of 0.40% or less [0.10% or less] after the "Hygroscopicity-Test Method" in the specification of the '615 patent at 22:56-64 [or the '796 patent at 22:59-67; or the '760 patent at 22:56-64].	*Indefinite (i.e., the claim, even read in light of the specification and the prosecution history, fails to inform, with reasonable certainty, those skilled in the art concerning the scope of the invention)*

Otsuka and Defendants (other than Teva, Prinston, Zydus, Aurobindo, and Amneal) substantively agree that a person of ordinary skill in the art would look to the specification of the '615, the '796, and the '760 Patents, in order to guide their understanding of the disputed claim phrase. (See, e.g., Otsuka's Opening Claim Constr. Br. at 18-19; Otsuka's Responsive Claim Constr. Br. at 19-20; Defs.' Responsive Claim Constr. Br. at 17; Markman Hr'g Tr. at 63:18-22.) These parties rely, in particular upon the following portion of the specifications:

> (7) **Hygroscopicity-Test Method**
> One g of the sample was accurately weighed in a weighing bottle (diameter 5 cm), covered with kimwipes and left to rest in a 60° C/100% RH environment

[42] Defendants proposing this construction consist of all of the generic defendants, except for Teva, Prinston, Aurobindo, and Amneal.

[43] Except with respect to the '615 Patent, which Otsuka has not asserted against Teva.

> (water/dessicator). 24 hours later, the weighing bottle was removed, transferred to an environment of a room temperature and about 30% RH (magnesium chloride hexahydrate saturated water solution/dessicator) and left to rest for 24 hours and the water content of the sample was measured by the Karl Fischer method.

(See '615 Patent at 22:56-64 (emphasis added); '796 Patent at 22:59-67; '760 Patent at 22:56-64.)

More specifically, these parties agree that because the disputed claim phrase defines the novelty of reduced hygroscopicity, it necessarily incorporates the "Hygroscopicity-Test Method" described by the specification. These parties diverge, however, on whether the specification should be read to account for "'reasonable variations' in the 'Hygroscopicity-Test Method'" (as argued by Otsuka), or whether the specification should be read as the strict definition of the disclosed test method (as argued by Defendants).[44] Teva, Prinston, Zydus, Aurobindo, and Amneal (hereinafter, the "indefinite Defendants"), by contrast, argue that the phrase defines itself, and therefore requires no construction, much less the importation of a claim limitation from the specification (i.e., any incorporation of the "Hygroscopicity-Test Method"). (Defs.' Responsive Claim Constr. Br. at 19-23.)

[44] These Defendants additionally challenge Otsuka's construction to the extent it states that "wherein said low hygroscopicity..." has a plain and ordinary meaning. (Defs.' Responsive Claim Constr. Br. at 17.)

The asserted claims and the specification closely track in language, as reflected in the following illustration:

Claim Language	Specification
A pharmaceutical solid oral preparation comprising Anhydrous Aripiprazole Crystals B having low hygroscopicity and one or more pharmaceutically acceptable carriers, wherein said low hygroscopicity is a moisture content of [0.40%/0.10%] or less after placing said Crystals for 24 hours in a desiccator maintained at a temperature of 60 ° C and a humidity level of 100%...	(7) Hygroscopicity-Test Method One g of the sample was accurately weighed in a weighing bottle (diameter 5 cm), covered with kimwipes and left to rest in a 60° C/100% RH environment (water/dessicator). 24 hours later, the weighing bottle was removed, transferred to an environment of a room temperature and about 30% RH (magnesium chloride hexahydrate saturated water solution/dessicator) and left to rest for 24 hours and the water content of the sample was measured by the Karl Fischer method.

Given the substantive similarities, the Court finds that a person of ordinary skill in the art would recognize that the claim language itself contains both a definition of "low hygroscopicity" and an unmistakable reference to the "Hygroscopicity Test Method" in the specification.[45] See Phillips, 415 F.3d at 1313 ("Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in

[45] For the same reason, the Court rejects the indefinite Defendants' argument that reliance upon the specification for purposes of claim construction improperly imports a limitation from the specification. Indeed, the similarity in language makes plain that the patentee intended the specification to be relied upon as an elucidation of the asserted claim. See Silicon Graphics, Inc. v. ATI Techs., Inc., 607 F.3d 784, 792 (Fed. Cir. 2010) (generally noting that district courts may not rely upon the specification to import limitations into claims, "unless the specification makes clear that the patentee intends for the claims and the embodiments in the specification to be strictly coextensive") (internal quotation marks omitted).

the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification."). In that way, the specification simply explains, in greater detail and under a heading entitled "Hygroscopicity Test Method," the actual steps involved in testing the hygroscopicity of the claimed invention.[46] (See also Buckton Dec. at ¶¶ 25-26; Byrn Dep. at 182:6.)

For that reason, the Court will adopt Defendants' construction.[47]

---

[46] The indefinite Defendants argue that the disputed phrase fails on indefiniteness grounds, as evidenced by the fact that Otsuka's contention that "when considering the claimed low hygroscopicity test, a POSA would look to the Hygroscopicity Test Method in the specification ***and*** consider 'reasonable variations' to account for 'practical realties.'" (Defs.' Responsive Claim Constr. Br. at 23 (emphasis in original).) Nevertheless, because the Court will not adopted Otsuka's "reasonable variations" construction, as explained below, it need not reach the issue of indefiniteness. However, even if it did, the disputed claims provide more than enough information to disclose the scope of the claims (or, the meaning of low hygroscopicity) with reasonable certainty. (See Buckton Dep. at 167:15-18, 392:14-393:1 (setting forth Dr. Buckton's opinion that the term, when viewed through the lens of the specification, is reasonable clear).)

[47] The Court will not, however, incorporate the "reasonable variations" proposed by Otsuka. In advancing a construction that includes "reasonable variations in the test method," Dr. Byrn appears to envision a construction that accounts for "practical laboratory realities" (Byrn Dec. at ¶ 65), e.g., laboratory variations, or "[s]omething as simple as a truck driving by the building or power fluctuations." (Markman Hr'g Tr. at 30:24-31:3.) These sorts of laboratory conditions, however, have no place in the Court's construction, nor any actual rooting in the intrinsic record. (See Byrn Dep. at 256:6-7 (stating that the Court need not adopt "reasonable variations" as part of its construction).)

D. "aripiprazole drug substance"

The phrase "aripiprazole drug substance" appears in asserted claims 1 and 2 of the '760 Patent, a Patent that discloses, on its face, "an improved form of aripiprazole having reduced hygroscopicity." ('760 Patent at 1:21-23 (emphasis added).) In other words, the '760 Patent teaches a tablet.

The asserted claims, in turn, describe an "Aripiprazole drug substance of low hygroscopicity wherein said low hygroscopicity is a moisture content of [0.40%/0.10%] or less after placing said Crystals for 24 hours in a desiccator maintained at a temperature of 60° C and a humidity level of 100%." (Id. at 44:23-32.)

With respect to this claim term, the parties advance the following competing constructions:

Otsuka's, Teva's, Sun's, and Prinston's Proposed Construction	Defendants' Proposed Construction
The phrase "Aripiprazole drug substance" has its plain and ordinary meaning as understood by a person of ordinary skill in the art.	Aripiprazole active pharmaceutical ingredient prior to incorporation with other excipients in a drug product.

The parties' dispute on this claim term turns, in essence, upon whether "aripiprazole drug substance" refers only to the aripiprazole compound, aripiprazole in its finalized formulation, and/or aripiprazole in either capacity.[48] (See Markman Hr'g Tr. at 140:23-147:13.)

[48] As stated above, only Otsuka presented arguments on the term "aripiprazole drug substance."

Nevertheless, the Court finds that "aripiprazole drug substance" requires no elaborate interpretation. Indeed, claims 1 and 2 of the '760 Patent identify the claimed invention as "Aripiprazole drug substance of low hygroscopicity wherein said low hygroscopicity is a moisture content of [0.40%/0.10%] or less after placing said Crystals for 24 hours in a desiccator maintained at a temperature of 60 ° C and a humidity level of 100%." ('760 Patent at 44:23-32.) In that way, the language makes clear that the "Aripiprazole drug substance" claimed in the '760 Patent broadly describes aripiprazole as the active ingredient of the finalized formulation.[49] The formulation examples, in turn, teach that "[t]he following examples used aripiprazole drug substance made by first milling or pulverizing the conventional hydrate of aripiprazole and then heating it to form the anhydrous form (anhydrous aripiprazole crystals b)." (Id. at 40:43-46.) The specification therefore makes clear that "aripiprazole drug substance" also refers, more broadly, to the aripiprazole compound prior to incorporation into its final formulations.

As a result, the Court finds that a person of ordinary skill in the art would, upon reviewing the language of the '760 Patent in its entirety, conclude that "aripiprazole drug

[49] Nearly every relevant embodiment of the specification contains a similar disclosure. (See, e.g., '760 Patent at 5:64-7:62.)

substance" means a drug substance that consists of aripiprazole, either in pure chemical form or as the active chemical ingredient in finalized form. (See Byrn Dep. at 92:10-19.)[50]

E. "a/the pharmaceutical composition" / "in combination with"[51]

In its TRO Opinion, the Court addressed, at great length, the appropriate construction of the phrase "pharmaceutical composition," as recited in the asserted claims of the '350 Patent. See Otsuka, ___ F. Supp. 3d ____, 2015 WL 1782653, at *9-*13. In connection with the pending Markman submissions, Otsuka, in essence, requests that the Court revisit its "preliminary" TRO construction, but largely reiterates positions this Court previously rejected, and again ignores the explicit teachings of its own specification.[52] (See generally Otsuka's Opening Claim Constr. Br. at 21-26; Otsuka's Responsive Claim Constr. Br. at 26-34.) Defendants, by contrast, urge the Court to maintain its previous construction. (See, e.g., Defs.' Opening Claim Constr. Br. at 30-33

[50] Only Otsuka presented expert testimony in support of its proposed construction of "aripiprazole drug substance."
[51] As stated above, this disputed phrase appears in claims 1 through 18 of the '315 Patent.
[52] Indeed, Otsuka has only augmented its position on this disputed claim phrase through its submission of additional extrinsic evidence, namely, the expert declarations of Dr. Correll and Dr. Byrn. Otsuka no longer relies upon Dr. Bryan L. Roth, the expert Otsuka relied upon in connection with the TRO proceedings.

The Court finds no reason to depart from its preliminary, but otherwise comprehensive, construction, and again concludes that the disputed phrase requires no elaborate construction.[53] Indeed, the claim language leaves little to the imagination, and requires no more than "the application of the widely accepted meaning of commonly understood words." Phillips, 415 F.3d at 1314.

Indeed, the claims of the '350 Patent contain identical terms, all of which support this Court's prior construction, as illustrated below:

Claim	Term
1	A pharmaceutical composition comprising (a) aripiprazole in combination with (b) at least one serotonin reuptake inhibitor selected from citalopram, escitalopram and salts thereof.
2	A pharmaceutical composition comprising aripiprazole in combination with at least one serotonin reuptake inhibitor selected from citalopram and salts thereof.
3	A pharmaceutical composition comprising aripiprazole in combination with at least one serotonin reuptake inhibitor selected from escitalopram and salts thereof.
4-8	The composition of any one of claims 1, 2, 3...
9	A method of treating a mood disorder ... [through] administration of an effective amount of a pharmaceutical composition which comprise(s)[54]

[53] As a result, the Court incorporates by reference the relevant discussion in its prior decision. See Otsuka, ___ F. Supp. 3d ____, 2015 WL 1782653, at *9-*13.

[54] Otsuka argues that claim 9 supports Otsuka's proposed construction. Nevertheless, reviewing this claim through the spectre of the remaining claims make clear that the patentee

	aripiprazole in combination with (b) at least one serotonin reuptake inhibitor selected from the group consisting of citalopram, escitalopram and salts thereof.
10	A method of treating a mood disorder ... [through] administration of an effective amount of a pharmaceutical composition comprising aripiprazole in combination with at least one serotonin reuptake inhibitor selected from the group consisting of citalopram, and salts thereof.
11	A method of treating a mood disorder ... [through] administration of an effective amount of a pharmaceutical composition comprising aripiprazole in combination with at least one serotonin reuptake inhibitor selected from the group consisting of escitalopram, and salts thereof.
12-16	The method of any one of claims 9 to 11...
13	The method of any one of claims 9 to 11, wherein the pharmaceutical composition further comprises at least one pharmaceutically acceptable carrier.
14-16	The method of any one of claims 9 to 11...
17	The composition of claim 5...
18	The composition of claim 1...

('350 Patent at 28:64-30:48.)

Several features critically relevant to construction immediately emerge from even a cursory inspection of the plain

---

intended the "(s)" to be "(a)." Any other interpretation proves wholly inconsistent with the remaining claims, particular dependent claim 13. (Compare '350 Patent at 29:37-38, with 30:23-25.) Even more critically, Otsuka has not requested that the Court construe the term "comprise(s)," and the opportunity to do so has long since expired. For these reasons, the Court finds that claim 9 provides no support for Otsuka's construction.

claim language, namely, the consistent inclusion of "a pharmaceutical composition" in the singular, followed by grammatically uninterrupted identification of the composition's at least two component parts. See Credle v. Bond, 25 F.3d 1566, 1571 (Fed. Cir. 1994) (stating that "grammatical structure and syntax" of the claim can be important evidence for claim construction). Indeed, taken together, the phrases "a pharmaceutical composition" and "in combination with," when followed by an unequivocal delineation of the required parts, provide a clear indication that the asserted claims of the '350 Patent refer to a single pharmaceutical composition or dosage comprised of multiple active pharmaceutical ingredients. See, e.g., Research Plastics, Inc. v. Fed. Packaging Corp., 421 F.3d 1290, 1295 (Fed. Cir. 2005) ("[C]laim terms are presumed to be used consistently throughout the patent, such that the usage of a term in one claim can often illuminate the meaning of the same term in other claims."); see also Phillips, 415 F.3d at 1314 (noting that "the use of a term within the claim [can] provide a firm basis for construing the term").

The overall structure of the '350 Patent, throughout its various sequential components, then consistently and repeatedly teaches that the claimed invention concerns a single dosage form, comprised of two active ingredients.

Indeed, the ’350 patent describes the invention at the outset in its abstract as a “pharmaceutical composition” comprised of “(1) a carbostyril derivative,” either “aripiprazole or a metabolite,” together with “(2) a serotonin reuptake inhibitor,” e.g., citalopram and/or escitalopram, “in a [single] pharmaceutically acceptable carrier.” (See ’350 Patent at Abstract (emphasis added).) In the disclosure of the invention, the ’350 patent then reiterates that the claimed invention consists of at least two ingredients “in a pharmaceutically acceptable carrier.” (Id. at 2:66-6:17.)

Identical disclosures appear in the Detailed Description, which describes in detail the “first” and “second” ingredients, “contained,” “combined,” or “mixed” in the single “pharmaceutical composition.” (See, e.g., id. at 6:47-55, 10:52-57, 11:47-48 (“Combination of the First Ingredient with the Second Ingredient”), 13:56-62 (“the amounts of the first ingredient and the second ingredient to be contained in the pharmaceutical composition of the present invention...”), and 20:27-41 (describing aripiprazole in a combined administration with citalopram and/or escitalopram).) Indeed, the introduction of the Detailed Description states that, “[t]he pharmaceutical composition of the present invention comprises a first ingredient comprising a carbostyil derivative active as a dopamine-serotonin system stabilizer and a second ingredient

comprising a serotonin reuptake inhibitor, in a pharmaceutically acceptable carrier." (Id. at 6:47-51 (emphasis added).) In that regard, the syntax of the introduction alone indicates that the single "pharmaceutically acceptable carrier" describes and limits the preceding composition to a carrier, or dosage, comprised of two ingredients. Even more, however, the Detailed Description contains the following illustrative subheadings: "The Pharmaceutical Composition: The First Ingredient," i.e., aripiprazole, "The Pharmaceutical Composition: The Second Ingredient," i.e., a serotonin reuptake inhibitor, and "Combination of the First Ingredient with the Second Ingredient," i.e., a combination of aripiprazole and an SRI, and preferably "a combination of aripiprazole/citalopram." (Id. at 6:56, 10:52, 11:47-59.) Imbedded within these six columns, the Patent uniformly treats the claimed invention as a single "combination" dosage, and specifically delineates the preferred weight ratio "of the first ingredient to the second ingredient" as generally, "about 1 to 70 parts by weight, preferably about 1 to 30 parts by weight of the first ingredient and the second ingredient in the total amount on the basis of the pharmaceutical composition." (See id. at 11:58-59, 12:61-63, 13:59-61.)

The eighteen "non-limiting formulation examples of aripiprazole" then uniformly disclose formulations for "the

[claimed] tablet" that contain multiple active pharmaceutical ingredients, namely aripiprazole combined with at least one SRI, together in a single "tablet." (Id. at 20:46-25:17 (emphases added); see also 11:54-58 (setting forth a non-exhaustive list of the relevant SRIs).)

Otsuka does not genuinely dispute the volume and pervasiveness of these consistent intrinsic references to a composition in a single dosage form.[55] Rather, it submits that the Court's construction must take into account the undisputed extrinsic reality that psychiatrists do not, as a practical matter, prescribe single dosage forms of antipsychotics and antidepressants. (See, e.g., Markman Hr'g Tr. at 36:6-18,

[55] The Court rejects Otsuka's reliance upon isolated portions of the specification for the same reasons set forth in the TRO Opinion. See Otsuka, ___ F. Supp. 3d ____, 2015 WL 1782653, at *12-*13. Critically, these portions of the specification all identify alternative embodiments involving separate dosage forms, not the single composition otherwise disclosed in the plain claim language and throughout the remainder of the specification. (See, e.g., '350 Patent at 3:52-67, 14:10-21.) The Court need not credit alternative embodiments, particularly those that, as here, "contradict" the relevant claim language. TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc., 529 F.3d 1364, 1373 (Fed. Cir. 2008) (declining to include alternatively disclosed embodiment because it "would contradict the language of the claims"); see also Rolls-Royce, PLC v. United Techs. Corp., 603 F.3d 1325, 1334-35 (Fed. Cir. 2010) (omitting certain disclosed embodiments to avoid a construction that "outweighs the language of the claim."). Moreover, even if the Court accepted Otsuka's interpretation of these specific portions of the specification, the specification itself cannot be "a substitute for, nor can [it] be used to rewrite, the chosen claim language." SuperGuide Corp. v. DirectTV Enters., Inc., 358 F.3d 870, 875 (Fed. Cir. 2004) ("[s]pecifications teach," "[c]laims claim").

104:9-105:7; Correll Dec. at ¶ 22.) Rather, psychiatrists prefer to engage in combination therapy, i.e., to prescribe an antipsychotic in a separate dosage form from the antidepressant, in order to have the ability to titrate the dosages based upon the individual reactions of certain patients. (See, e.g., Markman Hr'g Tr. at 36:6-37:11, 104:9-105:7.) Indeed, combination therapy appears to be the predominant method of treating mood disorders. (See Markman Hr'g Tr. at 104:18-20; Correll Dep. at 44:17-24 ("Combination therapy is more the rule than the exception in psychiatry, as it is in many areas of medicine, where one medication alone is not good enough.").) Nevertheless, the disputed claim phrase need not be construed in accordance with its most successful commercial form, and it remains true that there is at least one other commercially-successful product, Symbyax®, that combines "an atypical antipsychotic" with a "serotonin reuptake inhibitor," all while providing physicians the ability to titrate. [See Docket Item 200.] See also Chef Am., Inc. v. Lamb-Weston, Inc., 358 F.3d 1371, 1373 (Fed. Cir. 2004) ("[E]ven if, ... construing the patent ... produces a nonsensical result, the court cannot rewrite the claims. Plaintiff's patent could have easily been written to reflect the construction plaintiff attempts to give it today.")

The amount of intrinsic evidence that consistently discloses a single dosage form can hardly be described as anything less than substantial, and the Court again finds no support for Otsuka's position that the "pharmaceutical composition" identified by the '350 Patent should be construed to teach that aripiprazole and the at least one SRI (namely, escitalopram and/or citalopram) may be presented in separate and/or multiple dosage forms. For all of these reasons, the Court construes the phrase to refer to a single dosage form, or "pharmaceutical composition," containing at least two active ingredients: aripiprazole and at least one of citalopram, escitalopram and salt thereof.

V. CONCLUSION

An accompanying Order will be entered.

November 16, 2015
Date

s/ Jerome B. Simandle
JEROME B. SIMANDLE
Chief U.S. District Judge