IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

AMGEN INC., Plaintiff, v. AMNEAL PHARMACEUTICALS LLC, et al., Defendants.	)	Civ. No. 16-853-MSG CONSOLIDATED

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GOLDBERG, M., District Judge **JULY 26, 2018**

OPINION

I. INTRODUCTION

This is a consolidated patent infringement action arising under the Drug Price Competition and Patent Term Restoration Act of 1984, 21 U.S.C. § 355, also known as the Hatch-Waxman Act. United States Patent No. 9,375,405 (the "'405 patent") is assigned to Plaintiff Amgen Inc. ("Amgen") and listed in the Approved Drug Products with Therapeutic Equivalents (the "Orange Book") as covering Sensipar®. Amgen accuses multiple Defendants of infringing the '405 patent by filing Abbreviated New Drug Applications ("ANDAs") seeking FDA approval to manufacture, use and/or sell generic versions of Sensipar®. These Defendants are Amneal Pharmaceuticals LLC and Amneal Pharmaceuticals of New York LLC (collectively, "Amneal"), Piramal Healthcare UK Ltd. ("Piramal"), Watson Laboratories, Inc., Actavis, Inc., and Actavis Pharma, Inc. (collectively, "Watson"), and Zydus Pharmaceuticals (USA) Inc. and Cadila Healthcare Ltd. (collectively, "Zydus").

I bifurcated the infringement claims and invalidity counterclaims for trial, and held a four-day bench trial on infringement beginning on March 5, 2018. At the time of the pretrial conference, this case involved five additional defendants that have since entered into a consent judgment or stipulation of dismissal. (D.I. 316, D.I. 317, D.I. 320, D.I. 321, D.I. 348). Of those

five defendants, only one participated at trial: Aurobindo Pharma USA Inc. and Aurobindo Pharma USA, Inc., known collectively as "Aurobindo." Presently before me are the parties' post-trial proposed findings of fact and conclusions of law concerning infringement of the '405 patent. (D.I. 359, D.I. 360, D.I. 366, D.I. 367). I have subject matter jurisdiction over this matter pursuant to 28 U.S.C. §§ 1331 and 1338(a). Venue is proper in this court under 28 U.S.C. §§ 1391 and 1400(b).[1]

II. BACKGROUND

A. The '405 Patent

The '405 patent, entitled "Rapid Dissolution Formulation of Calcium Receptor-Active Compound," was issued by the United States Patent and Trademark Office ("Patent Office") on June 28, 2016. (D.I. 293, Ex. 1 at ¶ 5). The patent issued from U.S. Patent Application No. 12/942,646 (the "'646 application"), filed on November 9, 2010, and claims priority to U.S. Provisional Patent Application No. 60/502,219, filed on September 12, 2003. (*Id*. at ¶¶ 7, 8). The '405 patent has two independent claims (claims 1 and 20) and twenty-one dependent claims. (JTX 2 at 13:18-15:3).

For most of the asserted claims, the parties' stipulated that a finding of infringement would depend on the findings for claim 1 of the '405 patent. (*See* D.I. 336). Claim 1 recites a pharmaceutical composition combining specific excipients in specific amounts with the active ingredient cinacalcet hydrochloride ("cinacalcet HCI"). Excipients are the inert ingredients used in drug formulations to perform specific functions, such as diluent, binder, or disintegrant. (JTX 11 at 2545). Diluents provide bulk to the formulation so that the tablets are of sufficient size for

[1] On May 18, 2017, Chief Judge D. Brooks Smith of the United States Court of Appeals for the Third Circuit designated me as a visiting judge for the District of Delaware, pursuant to 28 U.S.C. § 292(b), to handle this and other Delaware cases.

handling. (PTX 454 at 404; D.I. 356 at 946:13-19). Binders act as the adhesive that holds the drug and excipients together. (D.I. 353 at 186:8-20). Disintegrants ensure the breakup of the tablet upon ingestion thereby promoting absorption of the drug substance. (JTX 11 at 2545; PTX 447 at 105). With that background in mind, claim 1 of the '405 patent specifically states:

> A pharmaceutical composition comprising:
>
> (a) from about 10% to about 40% by weight of cinacalcet HCl in an amount of from about 20 mg to about 100 mg;
>
> (b) from about 45% to about 85% by weight of a diluent selected from the group consisting of microcrystalline cellulose, starch, dicalcium phosphate, lactose, sorbitol, mannitol, sucrose, methyl dextrins, and mixtures thereof;
>
> (c) from about 1% to about 5% by weight of at least one binder selected from the group consisting of povidone, hydroxypropyl methylcellulose, hydroxypropyl cellulose, sodium carboxymethylcellulose, and mixtures thereof; and
>
> (d) from about 1% to 10% by weight of at least one disintegrant selected from the group consisting of crospovidine (sic), sodium starch glycolate, croscarmellose sodium, and mixtures thereof;
>
> wherein the percentage by weight is relative to the total weight of the composition, and wherein the composition is for the treatment of at least one of hyperparathyroidism, hyperphosphonia, hypercalcemia, and elevated calcium phosphorus product.

(JTX 2 at 13:18-39).

For reasons unknown to me, the parties' stipulation did not cover three of the dependent claims Amgen has asserted against various defendants. Those are claims 5, 6, and 18. Claim 5 recites, "The composition according to claim 1, wherein the at least one binder is povidone." (JTX 2 at 13:53-54). Claim 6 recites, "The composition according to claim 1, wherein the at least one disintegrant is crospovidone." (*Id*. at 13:55-56). Claim 18 recites, "The composition according to claim 1, wherein the hyperparathyroidism is primary hyperparathyroidism or secondary hyperparathyroidism." (*Id*. at 14:23-24).

B. Person of Ordinary Skill in the Art ("POSA")

The parties' definitions of a POSA do not meaningfully differ. (*See, e.g.*, D.I. 356 at 907:1-8; D.I. 353 at 183:5-16). A POSA should have an advanced degree with a M.S. or Ph.D. in chemistry, pharmacy and/or pharmacology or a related field, as well as work experience in drug dosage and formulations. (D.I. 356 at 939:17-940:4; *accord* D.I. 353 at 182:10-183:4).

C. Prosecution of the '405 Patent

1. The Original Claim

The '646 application was a continuation of U.S. Patent Application No. 10/937,870 (the "'870 application"). As originally-filed by Amgen, the '646 application contained one broad claim. (JTX 5 at SENS-AMG 47; D.I. 355 at 621:23-622:14). Claim 1 covered a "pharmaceutical composition comprising an effective dosage amount of a calcium receptor active compound and at least one pharmaceutically acceptable excipient." The claim further stated that the composition had a particular dissolution profile. (JTX 5 at SENS-AMG 47). But the dissolution profile has not been relevant in this litigation, except to note that the inventive feature of the '405 patent was a "rapid" dissolution profile for a poorly soluble drug. (*Id*. at SENS-AMG 520).

2. The 2011 Preliminary Amendment

Before the Patent Office took formal action on the original claim, Amgen filed a preliminary amendment on November 15, 2011 (the "2011 Preliminary Amendment") cancelling claim 1 and adding new claims 2 through 24. (JTX 5 at SENS-AMG 257-62). Claim 2 narrowed the scope of the claims by requiring specific amounts of three specific types of excipient—diluents, binders, and disintegrants—and further requiring that the diluent be selected from a Markush group. (*Id.*; D.I. 354 at 393:16-20). A Markush group "lists alternative species

or elements that can be selected as part of the claimed invention." *Multilayer Stretch Cling Film Holdings, Inc. v. Berry Plastics Corp*., 831 F.3d 1350, 1357 (Fed. Cir. 2016). It is typically expressed in the form: "a member selected from the group consisting of A, B and C." *Abbott Labs. v. Baxter Pharm. Prods., Inc*., 334 F.3d 1274, 1280 (Fed. Cir. 2003). New independent claim 2 read:

> A pharmaceutical composition comprising:
>
> (a) from about 10% to about 40% by weight of cinacalcet HCl;
>
> (b) from about 45% to about 85% by weight of a diluent selected from the group consisting of microcrystalline cellulose, starch, dicalcium phosphate, lactose, sorbitol, mannitol, sucrose, methyl dextrins, and mixtures thereof,
>
> (c) from about 1% to about 5% by weight of at least one binder; and
>
> (d) from about 1% to 10% by weight of at least one disintegrant, wherein the percentage by weight is relative to the total weight of the composition.

(JTX 5 at SENS-AMG 258). Claims 3 through 23 were dependent on claim 2; claim 24 was the same as claim 2 except without the Markush group. (*Id.*).

On September 16, 2014, the Patent Office issued a non-final Office Action rejecting claims 2 through 24 as obvious "over Van Wagenen (US 6,211,244 B1) as evidenced by Kajiyama et al. (US 6,656,492), in view of Creekmore (US 6,316,460 B1) and Hsu et al. (US 2005/0147670)." (JTX 5 at SENS-AMG 291-97). As the Examiner explained, Van Wagenen discloses compounds that "read on cinacalcet HCl" and "can be used to treat diseases such as primary hyperparathyroidism and secondary hyperparathyroidism." (*Id.* at SENS-AMG 293-94). Hsu discloses pharmaceutical formulations where eleven specific binders—including starch and all four binders in claim 1 of the '405 patent—may be present in an amount from about 1% to about 80% by weight. (*Id.*; PTX 11 at ¶¶ 17, 46). Hsu also discloses twelve specific disintegrants—including all three disintegrants in claim 1 of the '405 patent—that may be

present in an amount of about 0.1% to about 10% by weight. (JTX 5 at SENS-AMG 293-97; PTX 11 at ¶ 51). Creekmore discloses pharmaceutical formulations where nineteen binders—including starch, pregelatinized starch, and three of the four binders in claim 1 of the '405 patent—may be present in an amount of 2% to 90% by weight. (JTX 5 at SENS-AMG 295; PTX 7 at 2:32-43). Creekmore also discloses that eight disintegrants—including all three disintegrants in claim 1 of the '405 patent—may be present in an amount of about 2% to 10%. (JTX 5 at SENS-AMG 295; PTX 7 at col. 2-3).

3. The 2014 Amendment

On December 15, 2014, Amgen responded to the September 16, 2014 Office Action by filing an amendment (the "2014 Amendment") that narrowed the claims. (D.I. 354 at 394:20-395:1). Amgen amended independent claim 2 to add that the cinacalcet HCl must be present "in an amount of from about 20 mg to about 100 mg." (JTX 5 at SENS-AMG 308-318). Amgen argued to the Patent Office that the 2014 Amendment overcame the prior art references cited in the Office Action by adding a precise amount of cinacalcet HCI. (*Id.* at SENS-AMG 313-319).

4. The Examiner's Amendment

The Examiner did not allow the 2014 Amendment. (D.I. 354 at 398:2-7). Instead, on March 12, 2015, the Examiner had an interview with Amgen's counsel and proposed an Examiner's Amendment that further narrowed the claims. (JTX 5 at SENS-AMG 340). The Examiner's Amendment canceled dependent claims 6, 8, and 22 and imported those limitations into independent claim 2 (which later issued as claim 1). (*Id*. at SENS-AMG 333-338). Original claim 6 stated, "The composition according to claim 1, wherein the at least one binder is selected from the group consisting of povidone, hydroxypropyl methylcellulose, hydroxypropyl cellulose, sodium carboxymethylcellulose, and mixtures thereof." (*Id.* at SENS-AMG 310). Original

claim 8 stated, "The composition according to claim 1, wherein the at least one disintegrant is selected from the group consisting of crospovidine (sic), sodium starch glycolate, croscarmellose sodium, and mixtures thereof." (*Id.*). Original claim 22 was a treatment limitation. Thus, as proposed by the Examiner, amended claim 2 now read:

> A pharmaceutical composition comprising:
>
> (a) from about 10% to about 40% by weight of cinacalcet HCl in an amount of from about 20 mg to about 100 mg;
>
> (b) from about 45% to about 85% by weight of a diluent selected from the group consisting of microcrystalline cellulose, starch, dicalcium phosphate, lactose, sorbitol, mannitol, sucrose, methyl dextrins, and mixtures thereof,
>
> (c) from about 1% to about 5% by weight of at least one binder selected from the group consisting of povidone, hydroxypropyl methylcellulose, hydroxypropyl cellulose, sodium carboxymethylcellulose, and mixtures thereof; and
>
> (d) from about 1% to 10% by weight of at least one disintegrant selected from the group consisting of crospovidine, sodium starch glycolate, croscarmellose sodium, and mixtures thereof,
>
> wherein the percentage by weight is relative to the total weight of the composition, and wherein the composition is for the treatment of at least one of hyperparathyroidism, hyperphosphonia, hypercalcemia, and elevated calcium phosphorus product.

(*Id.* at SENS-AMG 333-34 (underlining Examiner's amendments)).

After Amgen agreed to the Examiner's Amendment, the Examiner found that the pending claims overcame the obviousness rejection. (JTX 5 at SENS-AMG 338). Thus, on March 25, 2015, the Patent Office issued a Notice of Allowance with three attachments: the Examiner-Initiated Interview Summary, the Examiner's Amendment, and the Examiner's Statement of Reasons for Allowance. (*Id*. at SENS-AMG 332). The Examiner's reasons for allowance stated:

> The closet [sic] prior art was that which was cited in the previous office action filed on 09/16/2014, but fails to specifically disclose or render obvious the combination of components and in the amounts thereof set forth in claim 2.

> The claimed subject matter is not taught or suggested by the cited reference and thus, the claimed subject matter are [sic] considered to be novel and patentably distinct over the prior art of the record.

(*Id.* at 338). Although there was additional prosecution after this first notice of allowance, the claims ultimately issued in the same form. Independent claims 2, 24, and 26 from the patent application issued as independent claims 1, 20, and 21, respectively. (*Id*.).

5. Additional Prosecution and Issuance of the '405 Patent.

After the Examiner allowed Amgen's claims, Amgen filed a series of Requests for Continued Examination ("RCE"). (JTX 5 at SENS-AMG 345-46, SENS-AMG 1092-93, SENS-AMG 1613-14). With each RCE, Amgen submitted Information Disclosure Statements identifying additional prior art and documents Amgen claimed were relevant to the prosecution of the '405 patent. (JTX 5 at SENS-AMG 348-1063, SENS-AMG 1095-1576, SENS-AMG 1611-12). None of Amgen's RCEs amended the claims or made further arguments for patentability. (*Id.*).

On December 1, 2015, while Amgen's second RCE was pending, Amgen submitted a preliminary amendment (the "2015 Preliminary Amendment"). (*Id.* at SENS-AMG 1577-86). In this amendment, Amgen re-submitted the claims as they appeared in the Examiner's Amendment, except Amgen underlined the Examiner's verbatim additions. (Compare JTX 5 at SENS-AMG 1578 (Amgen's Amendment), with *id*. at SENS-AMG 333-34 (Examiner's Amendment); *see also* D.I. 354 at 360:1-14). In the Remarks section of the document, Amgen's counsel stated that the "amendments have not been made in response to a prior art rejection but rather to place the claims in proper format and to better define the claimed subject matter, including equivalents." (*Id.* at SENS-AMG 1583). After each RCE and the 2015 Preliminary Amendment, the Examiner allowed the same claims as originally set forth in the Examiner's Amendment. The Examiner's statement of reasons for allowance identified "the amount of

cinacalcet HCl," "the nature of the excipients," and "their respective combinations." (*See* JTX 5 at SENS-AMG 1064-71, SENS-AMG 1587-95, SENS-AMG 1643-50, and SENS-AMG 1693).

D. Claim Construction

The court has construed three terms in claim 1 of the '405 patent. On July 19, 2017, the Honorable Gregory Sleet, who was first assigned to this matter, construed the term "relative to the total weight of the compositions" in accordance with its plain and ordinary meaning. (D.I. 186). On February 27, 2018, this case having been reassigned to me as a visiting judge, I construed the Markush groups for the binder and disintegrant elements as "closed to unrecited binders and disintegrants." (D.I. 300 at 6). I concluded that "there could be no literal infringement if the Defendants' ANDA product contained an unrecited (or unlisted) binder or disintegrant." (*Id*.). Thus, in order to prove literal infringement, Amgen must prove that all of the binders and disintegrants in a defendant's ANDA product are members of the respective Markush group. (*Id*. at 9).

Amgen opposed the court's construction of the Markush groups by filing a motion for reargument, which was denied. (D.I. 323, D.I. 358). Amgen also elicited testimony from its expert, Dr. Davies, and made arguments in its post-trial brief that were inconsistent with the controlling claim construction. (*See, e.g*., D.I. 354 at 283:4-18; *Id*. at 297:9-14; *Id*. at 457:8-15; D.I. 355 at 539:8-540:21; D.I. 359 at 25). "Once a district court has construed the relevant claim terms, and unless altered by the district court, then that legal determination governs for purposes of trial." *Exergen Corp. v. Wal-Mart Stores, Inc*., 575 F.3d 1312, 1321 (Fed. Cir. 2009). Thus, Dr. Davies' expert testimony regarding infringement will be disregarded where it was inconsistent with or "based on an incorrect understanding of the claim construction." *Cordis*

Corp. v. Boston Sci. Corp., 658 F.3d 1347, 1357–58 (Fed. Cir. 2011). In addition, I will not address Amgen's arguments that are based on a claim construction I have already rejected.[2]

Finally, I must correct Amgen's assertion in its post-trial brief that my opinion denying the motion for reargument held, as a matter of law, that any pregelatinized starch in a defendant's accused product "count[s]" only as a diluent. (D.I. 359 at 13, 17, 22). That opinion's discussion of pregelatinized starch was limited to the Example in the '405 patent. (*See* D.I. 357 at 9-11). In that opinion, I rejected Amgen's argument that the only way to give meaning to the Example was to construe claim 1 as open to unlisted binders. (*Id*.). As I explained, claim 1 of the '405 patent covers pregelatinized starch that functions as a diluent. (*Id*.). In addition, the '405 patent teaches that the pregelatinized starch in the Example is functioning as a diluent. (*Id*.). So, the '405 patent already covered the Example without having to construe the claim as open to unlisted binders. (*Id*.). What the '405 patent teaches about the Example, however, does not dictate how pregelatinized starch functions in a defendant's formulation. As every expert witness at trial testified, the particular function of pregelatinized starch in any given formulation depends on the context. (JTX 11 at 2548; PTX 438 at 686; D.I. 354 at 268:21-269:3; *Id*. at 309:21-22; *Id*. at 468:1-9; D.I. 355 at 504:14-505:1; *Id*. at 506:15-507:17; *Id*. at 510:2-11; *Id*. at 511:4-512:5; *Id*. at 584:19-585:5; D.I. 356 at 955:14-956:10; *Id*. at 1082:20-1083:15). My memorandum opinion on the motion for reargument was consistent with these scientific principles. Contrary to Amgen's assertion, I did not previously hold that the pregelatinized starch in a defendant's formulation counts only as a diluent.

[2] For example, Amgen argues that Opadry infringes the binder limitation, because the open-ended term "comprising" in claim 1 allows for unlisted excipients such as polyethylene glycol, and Opadry is an excipient made in part with polyethylene glycol. (D.I. 359 at 25).

III. CONCLUSIONS OF LAW

A. Standard

A patent is infringed when a person "without authority makes, uses, offers to sell, or sells any patented invention, within the United States ... during the term of the patent." 35 U.S.C. § 271(a). To provide jurisdiction over an infringement dispute before an ANDA applicant has actually made or marketed the proposed product, 35 U.S.C. § 271(e)(2) states that submission of an ANDA is an act infringement "if the purpose of such submission is to obtain approval . . . to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent . . . before the expiration of such patent." The filing of an ANDA alone does not prove infringement. *Glaxo, Inc. v. Novopharm, Ltd*., 110 F.3d 1562, 1570 (Fed. Cir. 1997). Rather, the patentee must show, using "traditional patent infringement analysis," that "the alleged infringer will likely market an infringing product." *Id*. at 1569-70; *see also Warner-Lambert Co. v. Apotex Corp*., 316 F.3d 1348, 1365–66 (Fed. Cir. 2003)

A traditional infringement analysis entails two steps. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). First, the court must determine the meaning and scope of the asserted claims. *Id*. Second, the trier of fact must compare the properly construed claims with the product accused of infringement. *Id*. The patent owner must show, by a preponderance of the evidence, that each and every limitation of the asserted patent claim is found in the accused product, either literally or by equivalent. *SmithKline Diagnostics, Inc. v. Helena Lab. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988).

B. Amneal

Amneal filed Abbreviated New Drug Application No. 204364 ("ANDA") with the FDA seeking approval to market a generic version of cinacalcet hydrochloride in 30, 60, and 90 mg

dosage strengths. (D.I. 293, Ex. 1 at ¶ 35). Amneal included a certification in its ANDA pursuant to 21 U.S.C. §355(j)(2)(A)(vii)(IV) (a "Paragraph IV Certification") stating that the '405 patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Amneal's product. (*Id*. at ¶ 36). Amgen claims that Amneal's product will infringe claims 1-4, 6, 8-12, and 14-18 of the '405 patent. (D.I. 293, Ex. 2 at ¶¶ 25-26). Amneal has stipulated that if its ANDA product infringes claim 1, then its ANDA product will also infringe claims 2-4, 8-12, and 14-17, to the extent each claim is found valid and enforceable. (D.I. 336 at ¶ 1). The stipulation did not cover the asserted claims 6 and 18.

According to the ANDA, Amneal's product has the following composition:[3]

Ingredient	**Function**
Cinacalcet HCl	Active
Mannitol	Diluent
Microcrystalline Cellulose	Diluent
Opadry Clear YS-1-7006	Binder
Crospovidone	Disintegrant
Pregelatinized Starch	Secondary Disintegrant

(PTX 183 at 42).

1. Binder

According to the ANDA, the only binder in Amneal's product is Opadry YS-1-7006 ("Opadry"). But claim 1 of the '405 patent does not list Opadry in the Markush group for binders, which means under my claim construction order, there is not a clear case of literal

[3] As is true for all defendants in this case, Amneal's pharmaceutical composition includes additional excipients not relevant to this litigation and, therefore, not discussed here.

infringement. Amgen nonetheless attempts to prove literal infringement by arguing that Opadry is a pseudonym for hydroxypropyl methylcellulose ("HPMC"), which is a listed binder. (D.I. 359 at 24-25). Alternatively, Amgen argues that infringement is established through the doctrine of equivalents. (*Id*. at 26-27). I disagree with Amgen on both of these arguments.

To start, I find that a POSA would not regard Opadry as a synonym or trade name for HPMC. Authoritative pharmaceutical handbooks relied on in the industry identify synonyms for excipients. (*See* PTX 438 at 326). Opadry is not one of the synonyms given for HPMC. (*Id*.). It was also common practice for the inventors of the '405 patent and Amneal's ANDA to list an excipient followed by its tradename in parenthesis. (*See, e.g.*, JTX 2 at 11:21-42 ("Microcrystalline cellulose (Avicel PH102)," "Povidone (Plasdone K29/32)," etc.); PTX 183 at 42 ("Mannitol, USP (Mannogem EZ)," "Microcrystalline Cellulose, NF (Vivapur Type 101)," etc.)). Whenever HPMC appears in the '405 patent, it is not followed by a reference to Opadry. (JTX 2 at 6:61, 7:30-31). The opposite is also true. Whenever the '405 patent or Amneal's ANDA mention Opadry, it is not linked to HPMC. (JTX 2 at 11:37, 11:39, 12:22, 12:23; PTX 183 at 42).

In addition, I conclude for numerous reasons that Opadry is not literally HPMC. The excipients have different chemical structures, physical characteristics, binding mechanisms, and commercial sources. HPMC is a single molecule, whereas Opadry is a molecular dispersion of three distinct chemical ingredients: HPMC, polyethylene glycol 400, and polyethylene glycol 8000. (D.I. 355 at 796:8-22; DTX-AMN 7 at 8). HPMC is "an off-white poorly flowing powder," whereas the three ingredients in Opadry make a "slurry." (D.I. 355 at 791:4-24). HPMC binds principally through adhesion, while Opadry binds principally through cohesion. (*Id*. at 796:23-797:9). Specifically, HPMC acts as a wet granulation binder by sticking different

types of particles together, forming a granule from the inside, out. (*Id.* at 797:2-5). But Opadry acts as a wet granulation binder by spreading and surrounding the drug and excipient particles, forming a granule from the outside, in. (*Id.* at 797:5-9). Opadry is a product manufactured by a single company, Colorcon, using a proprietary method, whereas HPMC is not. (*Id*. at 788:18-21). Given the above evidence, Amgen has failed to prove by a preponderance of the evidence that Opadry is actually HPMC. Because Opadry is an unlisted binder, Amneal does not literally infringe the binder limitation of claim 1.

Amgen also does not infringe the binder limitation under the doctrine of equivalents. A finding of infringement under the doctrine of equivalents requires a showing that: (1) "the difference between the claimed invention and the accused product or method was insubstantial," or (2) "the accused product or method performs the substantially same function in substantially the same way with substantially the same result as each claim limitation of the patented product or method." *AquaTex Indus., Inc. v. Techniche Solutions*, 479 F.3d 1320, 1326 (Fed. Cir. 2007). Regardless of which test is used, a patentee must "provide particularized testimony and linking argument on a limitation-by-limitation basis." *Id*. at 1328-29. "[W]hile many different forms of evidence may be pertinent, when the patent holder relies on the doctrine of equivalents, as opposed to literal infringement, the difficulties and complexities of the doctrine require that evidence be presented to the jury or other fact-finder through the particularized testimony of a person of ordinary skill in the art, typically a qualified expert." *Id*. at 1329.

Here, Amgen's expert, Dr. Davies, never once used the word "function," "way," "result," or "substantial/insubstantial differences." (*See* D.I. 354 at 263:14-268:11). Nor did he provide

particularized testimony on each point of comparison.[4] (*Id.*). Instead, Dr. Davies opined in conclusory fashion that only the HPMC fraction of Opadry functioned as the binder, and "the polyethylene glycol … in the Opadry doesn't act as a binder." (*Id*. at 267:11-18). The court is not obligated to accept the conclusory assertions of an expert. *Optical Disc Corp. v. Del Mar Avionics*, 208 F.3d 1324, 1336 n. 5 (Fed. Cir. 2000). Thus, Dr. Davies' opinion, given without explanation or corroborating evidence, is not persuasive.

In addition, Amneal presented persuasive evidence refuting Dr. Davies' opinion that polyethylene glycol does not contribute to the binding properties of Opadry. Amneal's expert, Dr. McConville, credibly testified that Opadry is a "co-process excipient," which means that "those excipients work together and can never be separated." (D.I. 355 at 794:2-5). In addition, the presence of the polyethylene glycol in Opadry changes the mechanism by which HPMC binds, because polyethylene glycol, which is a liquid substance, allows the HPMC in Opadry to move freely, spread, and coat the other particles. (*Id*. at 802:13-24). Scientific literature states that, in tablet formulations, polyethylene glycols "can enhance the effectiveness of tablet binders." (PTX 438 at 518). Testing by Amneal demonstrated results consistent with this scientific statement. A series of tests compared formulations using HPMC and Opadry as binders and found a "significant difference" in the rate of release. (PTX 183 at 61-65). From these tests, Amneal concluded that Opadry was "the best choice of binder to achieve enhanced drug release profile."[5] (*Id*. at 65). Dr. Davies admitted that his opinion did not consider or respond to these tests. (D.I. 354 at 484:23-491:5). For all of the reasons stated above, I conclude

[4] It was not until post-trial briefs that Amgen defined the function, way, or result of the purported equivalents. (*See* D.I. 359 at 26-27).

[5] Amneal tested one formulation that compared HPMC to Klucel and found "no significant difference" between the two binders. (PTX 183 at 62-64). Amgen then tested a second formulation that compared Klucel to Opadry and found "faster in drug release" with Opadry as a binder. (PTX 183 at 64-65).

that Amgen has not proven by a preponderance of the evidence that Opadry is equivalent to HPMC.

2. Disintegrant

Amneal's ANDA discloses the use of the listed disintegrant crospovidone and the unlisted disintegrant pregelatinized starch. (PTX 183 at 42). Under my claim construction order, there is no literal infringement if the ANDA formulation contains any unlisted disintegrant. (D.I. 300 at 6). The '405 patent lists "starch" in the Markush groups for diluents, and the parties remaining in this litigation do not dispute that the term "starch" in the '405 patent covers pregelatinized starch. (JTX 2 at 13:21-25). Accordingly, Amgen argues that the pregelatinized starch in Amneal's product is not functioning as a disintegrant, but as a diluent. (D.I. 359 at 28). Amgen's sole support for its argument is Dr. Davies' opinion that crospovidone is a super-disintegrant which destroys the structure of a tablet so quickly that the pregelatinized starch does not have the opportunity to act as a disintegrant. (D.I. 359 at 28; D.I. 354 at 269:4-10). For several reasons, I do not find Dr. Davies' opinion, as applied to Amneal's ANDA product, convincing.

First, as Dr. McConville testified, Amneal's ANDA product does not appear to need another diluent. A diluent is used to increase a tablet's size and weight. (D.I. 353 at 185:20-186:7). Amneal's ANDA product already includes two diluents—microcrystalline cellulose and mannitol—in a large amount; specifically, 67.89% by weight of the accused product. (PTX 183 at 42). Given the presence of two diluents in such a large amount, it does not make sense that Amneal would add a small amount (5.24%) of a third diluent. (D.I. 355 at 821:7-822:2).

Second, Dr. McConville persuasively testified that, with Amneal's manufacturing process, the crospovidone cannot usurp the disintegration function of the pregelatinized starch.

(*Id*. at 809:3-6). In tablet manufacturing, ingredients can be either inside the granule with the active drug (intragranular) or outside the granule (extragranular). (*Id*. at 810:1-5). A disintegrant "can be more effective if used both 'intragranularly' and 'extragranularly,'" because the extragranular disintegrant will rupture the tablet to expose the granules, and the intragranular disintegrant will rupture the granules into fine particles to expose the drug. (DTX 216 at 8; D.I. 355 at 815:13-19, 818:15-819:3). Fine particles dissolve more quickly which helps achieve a rapid rate of dissolution—a required feature of the '405 patent. (D.I. 355 at 819:3-6; D.I. 359 at 6). Here, Amneal uses pregelatinized starch as an intragranular disintegrant and crospovidone as an extragranular disintegrant. (PTX 183 at 74 & 80). Because the crospovidone is only present outside the granules, it cannot accomplish that second disintegration of granules into fine particles. (D.I. 355 at 820:5-10). And because the pregelatinized starch is the only disintegrant inside the granules, it alone acts as a secondary disintegrant.

Third, Amneal's ANDA contains the results of testing which confirm that the pregelatinized starch in its product functions as a secondary disintegrant. (*See* PTX 183 at 70-73). To select a secondary disintegrant, Amneal tested the intragranular use of corn starch, pregelatinized starch, and crospovidone. (*Id*.). Amneal found that tablets with intragranular pregelatinized starch were "comparable" to Sensipar® in drug release, whereas corn starch was "slower in drug release." (*Id*. at 71). Amneal further found that the combination of pregelatinized starch and crospovidone was "better than [a] high amount of Crospovidone alone." (*Id*. at 73). Thus, Amneal concluded that pregelatinized starch was "the best choice for secondary disintegrant to design a robust, immediate release tablet dosage form of Cinacalcet Hydrochloride." (*Id*. at 71). Dr. Davies admits that his opinion does not account for these tests. (D.I. 354 at 466:18-467:24). He also acknowledged that he is not aware of any experiments or

scientific literature showing that, in the presence of crospovidone, pregelatinized starch does not contribute to tablet disintegration. (*Id*. at 527:7-530:24).

For all of these reasons, I find Dr. Davies' opinion regarding the function of pregelatinized starch in Amneal's ANDA product is not well supported. Instead, I conclude, consistent with Dr. McConville's opinion, that the pregelatinized starch in Amneal's product functions as a disintegrant. Because pregelatinized starch is an unlisted disintegrant, Amneal does not infringe the disintegrant limitation of claim 1.

3. Conclusion

To prove infringement, Amgen had the burden to show by a preponderance of the evidence that Amneal's binder Opadry was either a listed member of the binder Markush group or equivalent to a listed member. Amgen has done neither. In addition, Amneal's accused product includes an unlisted disintegrant (pregelatinized starch) that functions as a disintegrant. Thus, Amgen has failed to show by a preponderance of the evidence that Amneal's accused product infringes the binder and disintegrant limitations of the '405 patent. For the foregoing reasons, Amneal does not infringe claim 1 of the '405 patent. This means, pursuant to the parties' stipulation, Amneal does not infringe claims 2-4, 8-12, and 14-17. (D.I. 336 at ¶ 1). This also means that Amgen has not proven by a preponderance of the evidence that Amneal infringed dependent claims 6 and 18. "One who does not infringe an independent claim cannot infringe a claim dependent (and thus containing all the limitations of) that claim." *Wahpeton Canvas Co. v. Frontier, Inc*., 870 F.2d 1546, 1552 n. 9 (Fed. Cir. 1989).

C. Watson

Watson filed Abbreviated New Drug Application No. 204377 ("ANDA") with the FDA, seeking approval to market a generic version of cinacalcet hydrochloride in 30, 60, and 90 mg

dosage strengths. (D.I. 293, Ex. 1 at ¶ 100). Watson included a Paragraph IV Certification in its ANDA stating that the '405 patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Watson's product. (*Id*. at ¶ 101). Amgen claims that Watson's product will infringe claims 1-6 and 8-20 of the '405 patent. (D.I. 293, Ex. 2 at ¶¶ 39-40). Watson has stipulated that if its ANDA product infringes claim 1, then its ANDA product will also infringe claims 2-4, 8-17, and 19-20, to the extent each claim is found valid and enforceable. (D.I. 336 at ¶ 4). The stipulation did not cover the asserted claims 5, 6, and 18.

According to the ANDA, Watson's product has the following composition:

Ingredient	**Function**
Cinacalcet HCl	Active
Microcrystalline Cellulose	Diluent
Povidone	Binder
Pregelatinized Starch	Binder / Disintegrant
Low Substituted Hydroxypropyl Cellulose (L-HPC)	Disintegrant

(PTX 368 at 27).

The parties dispute whether Watson's ANDA product infringes the binder and disintegrant limitations of claim 1. I need not address the binder limitation, however, because a finding of non-infringement can be based on the disintegrant limitation alone. Watson uses an unlisted disintegrant, low substituted hydroxypropyl cellulose ("L-HPC"), which under my claim construction order means there is no literal infringement. As a result, Amgen argues that L-HPC infringes claim 1 under the doctrine of equivalence. As noted previously, there are two tests for proving equivalence: the function-way-result test or the insubstantial differences test. *Mylan*

Institutional LLC v. Aurobindo Pharma Ltd., 857 F.3d 858, 866 (Fed. Cir. 2017). Amgen's infringement theories under the doctrine of equivalence have shifted since trial.

At trial, Amgen took the position that L-HPC is equivalent only to crospovidone and only under the function-way-result test. (*See* D.I. 353 at 81:2-5 (Amgen's counsel stating in opening arguments that the evidence will show that L-HPC "is the equivalent to crospovidone."); D.I. 356 at 1089:5-7 (Amgen's counsel stating in closing arguments that the evidence has shown that "L-HPC is an equivalent to crospovidone."); D.I. 355 at 552:3-10 (Dr. Davies admitting that his opinions in this case rely only on the function-way-result test.). However, in its post-trial briefs, Amgen takes two new positions: (1) L-HPC is equivalent to all three listed disintegrants of claim 1 under the function-way-result test, and (2) L-HPC is equivalent to crospovidone under the insubstantial differences test.[6] (D.I. 359 at 32-36). Watson correctly points out that Amgen did not fairly present these positions in expert discovery or at trial. (D.I. 360 at 55). For that reason alone, Amgen's new infringement theories should be disregarded as an unfair surprise. Nevertheless, I will address Amgen's new infringement theories as presented in its post-trial briefs. Crospovidone is one of the three listed disintegrants in claim 1. Thus, in explaining why Amgen's new theories under the function-way-result test are not persuasive, I will necessarily explain why Amgen's original theory also would have failed.

1. Function-Way-Result Test

Amgen claims that L-HPC, a disintegrant listed in Watson's ANDA, is equivalent under the function-way-result test to all three listed disintegrants of claim 1. (D.I. 359 at 32-35). The three disintegrants listed in the Markush group of claim 1 are sodium starch glycolate,

[6] Amgen also makes the new argument in its post-trial briefs that L-HPC is "insubstantially different from [all of] the claimed disintegrants." (D.I. 359 at 32). Because Amgen provided no argument on this point besides this one sentence, I will not address it. It was not fairly presented to the court.

croscarmellose sodium, and crospovidone. (JTX 2 at 13:31-34). Under the function-way-result test, the patentee must show that the alleged equivalent "performs substantially the same function, in substantially the same way, to achieve substantially the same result, as disclosed in the claim." *Abbott Labs. v. Sandoz, Inc*., 566 F.3d 1282, 1296 (Fed. Cir. 2009).

The patentee should present its evidence on the doctrine of equivalence through the particularized testimony of an expert or person skilled in the art. *AquaTex*, 479 F.3d at 1329. Thus, Amgen should have presented through its expert, Dr. Davies, particularized testimony regarding the function, way, and result for each disintegrant to be compared. Dr. Davies, however, did not identify at trial what he considered to be the function, way, or result of the disintegrants being compared. (*See* D.I. 354 at 289:20-322:6). Instead, Amgen relies on a brief assertion by Dr. Davies that the disintegrants listed in claim 1 are "superdisintegrants," and L-HPC is "another superdisintegrant" with "similar disintegrant capability to other superdisintegrants." (*Id*. at 295:4-15). This testimony does not satisfy Amgen's burden to present the particularized testimony of an expert regarding the function, way, and result of the disintegrants being compared. Accordingly, Amgen failed to prove at trial that L-HPC is equivalent under the function-way-result test to all three disintegrants listed in claim 1.

Amgen's arguments in its post-trial brief fare no better. Amgen must show that L-HPC, sodium starch glycolate, croscarmellose sodium, and crospovidone perform substantially the same function, in substantially the same way, to achieve substantially the same result. According to Amgen, the function of L-HPC and the three listed disintegrants is to act as "superdisintegrants." (*See* PTX 359 at 9 (stating the disintegrants in claim 1 "function as superdisintegrants"); *Id*. at 32 (stating that "L-HPC functions as a superdisintegrant")). Scientific literature supports Dr. Davies' opinion that the three listed disintegrants are

superdisintegrants, but that same literature disproves Dr. Davies' assertion that L-HPC would be known by a POSA as a "superdisintegrant." According to scientific literature, L-HPC was one of the earliest known disintegrants upon which the new generation of disintegrants, known as superdisintegrants, improved. (JTX 11 at 2546; JTX 12 at 2155; DTX 334 at 235). Thus, the term "superdisintegrants" by its nature is used to distinguish the three disintegrants listed in claim 1 from the L-HPC used in Watson's product. (D.I. 355 at 669:14-670:6). Because L-HPC is not a superdisintegrant, it does not perform substantially the same function as the disintegrants listed in claim 1.

Amgen claims that L-HPC and the three listed disintegrants perform in substantially the same way, because they all use the same mechanism of disintegration: swelling.[7] (D.I. 359 at 32; D.I. 354 at 305:9-12). There is no dispute that the primary mechanism of action for L-HPC is swelling. (D.I. 355 at 671:7-9; DTX 324 at 2). But Amgen has not proven that the primary mechanism of action for each of the three listed disintegrants is swelling. For two of the three disintegrants—sodium starch glycolate and croscarmellose sodium—Amgen presented no evidence to corroborate Dr. Davies' testimony that the primary mechanism of action is swelling. (D.I. 359 at 32-33). In addition, Dr. Davies' testimony on this point was unclear: He also testified that "there are a number of different mechanisms by which [superdisintegrants] work." (D.I. 355 at 517:20-518:1). For the third listed disintegrant—crospovidone—Watson's expert, Dr. Appel, gave persuasive testimony, corroborated by scientific literature, that the primary mechanism of action is not swelling, but the recovery of elastic energy of deformation, also

[7] "Swelling is associated with dimensional amplification where particles enlarge omni-directionally to push apart the adjoining components, thereby initiating the break-up of the tablet matrix." (JTX 11 at 2546).

known as "strain recovery."[8] (*Id*. at 658:8-659:4, 668:3-20). Dr. Appel further testified that if swelling contributed to the disintegration mechanism of crospovidone it would play only a "minor role." (*Id*. at 725:20-726:12).

Scientific literature explains that initially there was no consensus regarding the primary mechanism of action for crospovidone, and researchers initially proposed swelling and wicking.[9] (JTX 11 at 2550). Since then, however, strain recovery has been "proposed and validated" as the "dominating disintegrant mechanism" of crospovidone. (*Id*.). Swelling makes only a "minor contribution." (DTX 334 at 239; *see also* JTX 12 at 2162 ("recovery of strain-energy … is the major mechanism of disintegrant action of crospovidone and not capillarity wicking or swelling")). I accept and credit this updated literature. Accordingly, Amgen has not proven that L-HPC and the three listed disintegrants perform in substantially the same way.

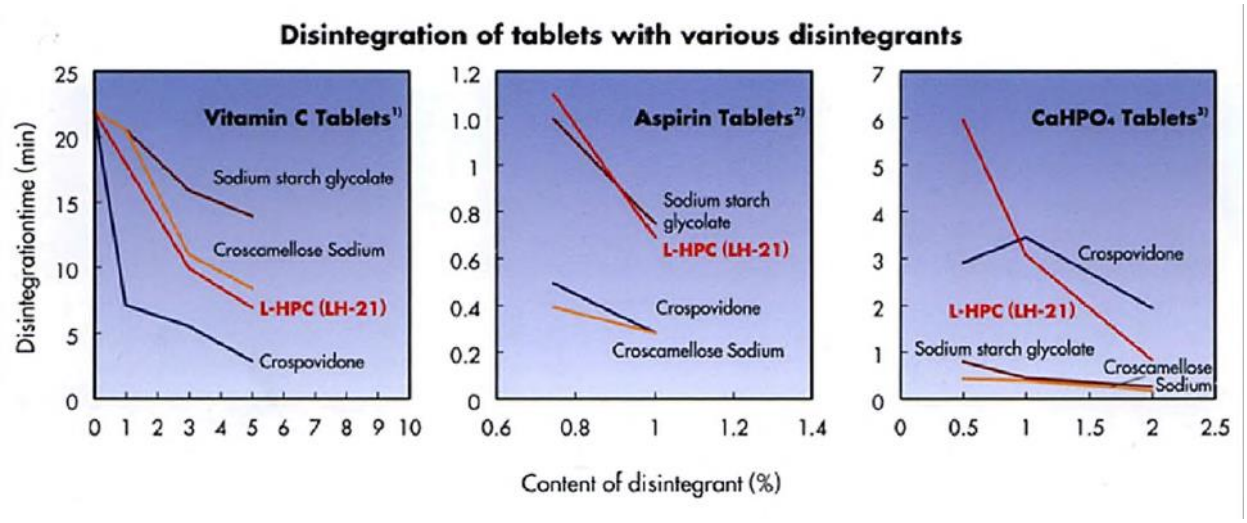
Finally, Amgen asserts that L-HPC and the three listed disintegrants achieve substantially the same result: "rapid tablet disintegration." (D.I. 359 at 32). Amgen's assertion, however, rests on a single sentence in a marketing brochure from the chemical company Shin Etsu stating: "L-HPC has similar disintegration capability to the other 'superdisintegrants.'" (*Id*. at 33; D.I. 354 at 295:4-19; PTX 463 at 12). A marketing brochure is not a peer reviewed scientific article and its goal is to sell a product, in this case L-HPC. (D.I. 355 at 673:24-675:20).

In addition, the marketing brochure itself calls into doubt Amgen's assertion. The brochure includes the caveat that the actual disintegration capability of various disintegrants "is

[8] To describe strain recovery, Dr. Appel used the analogy of a compressed spring returning to its original form. (D.I. 355 at 659:2-13; *see also* JTX 11 at 2548 and JTX 12 at 2155-56 (providing further detail on how the strain recovery mechanism operates in crospovidone)).

[9] Wicking may be defined as a process of liquid entry by capillarity into the microstructured crevices within the compact to displace the air. (JTX 11 at 2547).

dependent on [the] active ingredient and formulation." (PTX 463 at 12). The brochure illustrates its point with several graphs, reproduced below.



(*Id.*). Each graph represents a tablet with a different active ingredient. (D.I. 355 at 685:14-688:10). For each tablet, the graph compares the disintegration rates of L-HPC to the three superdisintegrants. (*Id.*).

Notably, the lines representing the rate of disintegration do not follow the same path and, at least for the CaHPO Tablets, do not even follow the same general direction. (*Id.* at 688:11-693:23). In addition, for Vitamin C tablets, crospovidone disintegrated at the fastest rate and sodium starch glycolate disintegrated at the slowest rate. (*Id.*). But for CaHPO4 tablets, the rankings flipped; sodium starch glycolate disintegrated at a faster rate than crospovidone. (*Id.*). Thus, two conclusions can be drawn from these graphs. One, L-HPC does not necessarily disintegrate at substantially the same rate as the superdisintegrants. (*Id.*). Two, it cannot be shown that L-HPC provides disintegration rates substantially similar to the superdisintegrants without testing involving the active ingredient at issue here, which is cinacalcet HCI. (D.I. 354 at 433:10-19). Amgen, however, did not present any tests or scientific literature that have made

this comparison.[10] Thus, Amgen has not proven that L-HPC achieves substantially the same result as all three listed disintegrants. Given the foregoing, Amgen has not proven by a preponderance of the evidence that L-HPC is equivalent to all three listed disintegrants under the function-way-result test.

2. Insubstantial Differences Test

Amgen argues that L-HPC is equivalent to crospovidone under the insubstantial differences test. (D.I. 359 at 36). The Federal Circuit has recognized that the function-way-result test can obscure important chemical differences and, therefore, advised that "the substantial differences test may be more suitable than [the function-way-result test] for determining equivalence in the chemical arts." *Mylan*, 857 F.3d at 867-69. Under the insubstantial differences test, "[a]n element in the accused product is equivalent to a claimed element if the differences between the two elements are 'insubstantial' to one of ordinary skill in the art." *Wi-Lan, Inc. v. Apple, Inc.*, 811 F.3d 455, 463 (Fed. Cir. 2016). Amgen's expert, Dr. Davies, did not provide an opinion regarding the insubstantial differences between L-HPC and crospovidone. (*See* D.I. 355 at 552:3-10 (Dr. Davies admitting that "[his] opinions in this case are entirely using the function way result test.")). Thus, the only particularized testimony in the trial record regarding the differences between L-HPC and crospovidone was presented by Watson's expert, Dr. Appel. She identified several differences between L-HPC and crospovidone, which were corroborated by scientific literature.

[10] Amgen's comparison of a disintegration test in Watson's Lab Notebook to a disintegration test in Watson's ANDA is not adequate for these purposes, because the formulations used different amounts of each excipient. (D.I. 359 at 33-34; PTX 368 at 27 & 50; PTX 391 at WTS-CNCLT-00173157 & 173159). Most noticeably, the intragranular disintegrant was almost doubled (6.66 mg compared to 10.20 mg) and the extragranular disintegrant was almost halved (16.20 mg compared to 9.75 mg). (PTX 368 at 27; PTX 391 at WTS-CNCLT-00173157). As Dr. Appel testified, a POSA would see these as two different formulations. (D.I. 355 at 740:3-741:14).

First, as Dr. Appel explained, L-HPC and crospovidone have different physical shapes. (D.I. 355 at 655:20-656:11). The physical shape of the particles affects how particles flow. (*Id*.). Particle flow "plays a crucial role" in pharmaceutical manufacturing, because "good flowability" ensures that the tablets' contents are uniform and consistent. (DTX 324 at 4; D.I. 355 at 655:20-656:11). Crospovidone particles are spherical "like marbles," whereas L-HPC particles are long and narrow "like spaghetti noodles." (D.I. 355 at 655:13-656:5; PTX 438 at 209 & 323). "Marbles flow really well," whereas spaghetti noodles "don't really flow well." (D.I. 355 at 655:13-656:5; *see also* DTX 324 at 1 (stating that L-HPC "showed poor flow properties" due to its high aspect ratios)).

Second, crospovidone and L-HPC have different chemical structures. Crospovidone is a five-member ring with four carbons and one nitrogen. (D.I. 355 at 653:1-7; PTX 438 at 208). L-HPC is a six-member ring with five carbons and one oxygen. (D.I. 355 at 653:1-15; PTX 438 at 322). Crospovidone is cross-linked, whereas L-HPC is not. (D.I. 355 at 661:22-662:18, 664:4-5). According to Dr. Appel, these differences mean a POSA would not consider L-HPC and crospovidone "as equivalent chemically." (*Id*. at 652:22-653:15).

Third, L-HPC is multi-functional, whereas crospovidone is not. (*Id*. at 656:15-22, 671:14-16). L-HPC can act as a binder or disintegrant, whereas crospovidone functions only as a disintegrant. (PTX 438 at 208 & 322). A POSA must take into account the multifunctional nature of an excipient, because the specific function such excipient will perform in any given formulation depends on the manufacturing process and the other excipients present. (D.I. 355 at 656:22-658:7; D.I. 354 at 268:21-269:3).

Fourth, when acting as a disintegrant, L-HPC is less potent than crospovidone. (*Id*. at 666:7-23; DTX 334 at 240 (stating that L-HPC "is not as effective as" crospovidone); JTX 12 at

2155 (explaining that crospovidone is "more efficient" than L-HPC)). Crospovidone levels are usually in the 2-5% range, and higher levels may cause problems, whereas L-HPC levels are typically in the 2-10% range, but can be higher. (DTX 334 at 239-40; D.I. 355 at 665:14-666:19). Given all of the foregoing evidence, Dr. Appel has credibly opined that L-HPC and crospovidone have differences that a POSA would find substantial. (D.I. 355 at 647:18-648:6, 653:19-654:7). Therefore, Amgen has not carried its burden of showing that L-HPC is equivalent to crospovidone under the insubstantial differences test.

3. Conclusion

Amgen has failed to prove by a preponderance of the evidence that L-HPC is equivalent to all of the disintegrants listed in claim 1 under the function-way-result test or that L-HPC is equivalent to crospovidone alone under the insubstantial differences test. Therefore, Watson does not infringe claim 1 of the '405 patent. This means, per the parties' stipulation, Watson does not infringe claims 2-4, 8-17, and 19-20. (D.I. 336 at ¶ 4). This also means, per *Wahpeton Canvas*, Watson does not infringe claims 5, 6, and 18. *Wahpeton Canvas*, 870 F.2d at 1552 n. 9 ("One who does not infringe an independent claim cannot infringe a claim dependent (and thus containing all the limitations of) that claim.").

D. Piramal

Piramal filed Abbreviated New Drug Application No. 210207 ("ANDA") with the FDA, seeking approval to market a generic version of cinacalcet hydrochloride in 30, 60, and 90 mg dosage strengths. (D.I. 293, Ex. 1 at ¶ 80). Piramal included a Paragraph IV Certification in its ANDA stating that the '405 patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Piramal's product. (*Id.* at ¶ 81). Amgen claims that Piramal's product will infringe claims 1-6 and 8-20 of the '405 patent. (D.I. 293, Ex. 2 at ¶¶ 35-

36). Piramal has stipulated that if its ANDA product infringes claim 1, then its ANDA product will also infringe claims 2-4, 8-17, and 19-20, to the extent each claim is found valid and enforceable. (D.I. 336 at ¶ 3). The stipulation did not cover the asserted claims 5, 6, and 18.

According to the ANDA, Piramal's product has the following composition:

Ingredient	**Function**
Cinacalcet HCl	Active
Corn / Maize Starch	Diluent
Microcrystalline Cellulose	Diluent
Pregelatinized Starch	Binder
Crospovidone	Disintegrant

(PTX 494 at PIR 229).

The parties dispute whether Piramal's ANDA product infringes the binder and disintegrant limitations of claim 1. A finding of non-infringement, however, can be resolved on the binder limitation alone. Amgen argues that the unlisted binder in Piramal's ANDA product—pregelatinized starch—has two components; a native starch fraction that actually functions as a diluent; and a cold water soluble fraction that functions as a binder. (D.I. 359 at 18-21). Neither pregelatinized starch nor its cold water soluble fraction are listed in the Markush group for binders, which under my claim construction order means there is no literal infringement. Accordingly, Amgen argues that cold water soluble fraction is equivalent to povidone. (*Id*.). For the reasons explained below, however, I find that Amgen is foreclosed by prosecution history estoppel from asserting the doctrine of equivalents against Piramal's use of pregelatinized starch as a binder.

1. Prosecution History Estoppel Applies

Prosecution history estoppel prevents a patent owner from using the doctrine of equivalents to recapture subject matter surrendered to acquire the patent. *Honeywell Int'l v. Hamilton Sunstrand Corp*., 523 F.3d 1304, 1312 (Fed. Cir. 2008). A presumption arises that the patent owner surrendered all equivalents in "the territory between the original claim and the amended claim" where: (1) an amendment narrows the scope of the claims, and (2) the amendment is adopted for a substantial reason related to patentability. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co*., 535 U.S. 722, 740 (2002). Amgen does not dispute that the Examiner's Amendment was a narrowing amendment. (*See* D.I. 359 at 49; D.I. 354 at 400:8-13, 402:19-22). Thus, the only issue here is whether the Examiner's Amendment was adopted for substantial reasons related to patentability. I find that it was.

Amgen tried—and failed—to overcome an obviousness rejection by making only one change to the claims: in the 2014 Amendment, Amgen narrowed the amount of cinacalcet HCl to "about 20 mg to about 100 mg." (JTX 5 at SENS-AMG 309, 316-17). The Examiner did not allow the claims in the 2014 Amendment. Instead, the Examiner proposed the Examiner's Amendment, which added the Markush groups to the binder and disintegrant limitations. (*Id*. at SENS-AMG 328-340). It was only after Amgen agreed to the entry of the Examiner's Amendment that the Examiner allowed the claims over the prior art. (*Id*.). There would have been no need for the Examiner to propose an amendment if Amgen's 2014 Amendment was sufficient. In addition, the Examiner expressly stated that he was allowing the claims as set forth in the Examiner's Amendment because, inter alia, the closest prior art "fails to specifically disclose or render obvious the *combination of components* and in the amounts thereof." (*Id*. at SENS-AMG 338). The Examiner's reliance on the "combination of components" underscores

the fact that the precise amount of cinacalcet HCI proposed in the 2014 Amendment was not enough by itself to overcome the obviousness rejection.

In addition, the Examiner's Amendment employed recognized methods for overcoming an obviousness rejection.[11] Original dependent claims 6 and 8 were canceled and the limitations in those claims—which were the Markush groups for binders and disintegrants respectively—were imported into now independent claim 1. *See, e.g.*, *Ranbaxy Pharm. Inc. v. Apotex, Inc*., 350 F.3d 1235, 1240 (Fed. Cir. 2003) (where patentee rewrote dependent claims into independent form, amendment was made for a substantial reason related to patentability); *Mycogen Plant Science, Inc. & Agrigenetics, Inc. v. Monsanto Co*., 261 F.3d 1345, 1350 (Fed. Cir. 2001) (finding that prosecution history estoppel applies where limitations were imported into independent claims from original dependent claims). At the same time, the Markush groups in claim 1 of the '405 patent resulted in fewer combinations of excipients than disclosed in the prior art. Creekmore disclosed 19 binders and 8 disintegrants, resulting in 152 combinations. (PTX 7 at 2:32-43; D.I. 355 at 633:10-21). Hsu disclosed 10 binders and 12 disintegrants, resulting in 120 combinations. (PTX 11 at ¶¶ 17, 46, 51; D.I. 355 at 633:22-634:11). The Examiner's Amendment disclosed a closed group of 4 binders and 3 disintegrants that resulted in 12 combinations. (D.I. 355 at 634:12-635:22). An obviousness rejection can be overcome by narrowing a claim to a smaller set of members within a group. *See, e.g.*, *Ranbaxy*, 350 F.3d at 1240-41 (limiting "highly polar solvent" to a "defined group of solvents" overcame obviousness rejection); *Merck & Co. v. Mylan Pharm. Inc*., 190 F.3d 1335, 1340-41 (Fed. Cir. 1999) (broad claims to polymers narrowed to specific polymers). For all of these reasons, I find that the

[11] Amgen argues that the Examiner's Amendment did not overcome the obviousness rejection. (D.I. 359 at 60-65). However, a patentee "may not both make the amendment and then challenge its necessity in a subsequent infringement action on the allowed claim." *Bai v. L&L Wings, Inc*., 160 F.3d 1350, 1356 (Fed. Cir. 1998).

Examiner's Amendment was adopted for substantial reasons related to patentability. Amgen's arguments to the contrary are unpersuasive.

First, Amgen relies heavily on its counsel's remark in the 2015 Preliminary Amendment that the "amendments have not been made in response to a prior art rejection but rather to place the claims in proper format and to better define the claimed subject matter." (D.I. 359 at 58-59; JTX 5 at SENS-AMG 1583). There is no reason to read this statement as describing anything more than the reason behind the 2015 Preliminary Amendment. Amgen itself states that "proper format" means the underlining added to show the changes made to the 2014 Amendment by the Examiner's Amendment, which is exactly what the 2015 Preliminary Amendment did. (D.I. 359 at 46 & 54). Thus, I find that a self-serving remark by Amgen's counsel in the 2015 Preliminary Amendment does not explain the reasons why Amgen agreed to the Examiner's Amendment over eight months earlier.

Second, Amgen relies heavily on the Examiner's statement in the second, third, and fourth notices of allowance that he was allowing the claims due to, inter alia, "the nature of the excipients." (D.I. 359 at 59). It is not clear from the record whether the phrase "nature of the excipients" means the genus of excipients (e.g., binder, diluent, etc.) or the species of excipients (e.g., sucrose, povidone, etc.). Nevertheless, when the Examiner described in the rejection the prior art that the claims failed to overcome, he explicitly pointed to the disclosure of specific excipients in specific functions. (*See*, *e.g.*, JTX 5 at SENS-AMG 295 (stating that Creekmore discloses "one or more fillers like microcrystalline cellulose," "one or more binders like starch," and "one or more disintegrants like polyvinylpyrrolidone (povidone)"); *Id*. (stating that Hsu discloses "binders like starch," "diluents like microcrystalline cellulose," and "disintegrants such as crospovidone")). When the Examiner first allowed the claims in the '405 patent, he explained

that the "combination of components … was not taught or suggested by" the prior art and is, therefore, "patentably distinct over the prior art." (JTX 5 at SENS-AMG 338). Thus, the Examiner very much had in mind the species of excipients when he decided that adding the Markush groups to claim 1 overcame the prior art. No further amendments or arguments were made after the first notice of allowance. So the later notices of allowance provide no additional insight into the reasons for the Examiner's Amendment.

Third, Amgen argues that if the Examiner's Amendment had been necessary for patentability, the Examiner would have checked one of the boxes in the Interview Summary form under the "Issues Discussed" section. (D.I. 354 at 348:4-349:20; D.I. 359 at 42). Several of the boxes are for common statutory bases used to reject claims: 35 U.S.C. § 101 (patent eligibility), § 112 (enablement), § 102 (novelty), and § 103 (obviousness). (JTX 5 at SENS-AMG 340). One box is for "Others" which, if checked, may have affirmatively indicated that some issue unrelated to patentability was discussed during the interview. (*Id*.). Here, none of the boxes were checked. (*Id*.). Accordingly, the boxes themselves provide no evidence either way regarding whether the amendment was made for reasons of patentability. It is also of no moment that none of the boxes are checked. The Manual of Patent Examining Procedure (the "MPEP") permits the Examiner to state his reasons for allowance in the Examiner's Amendment and not the Interview Summary Form. (*See* MPEP § 713 ("For an examiner-initiated interview, it is the responsibility of the examiner to make the substance of the interview of record either on an Interview Summary form *or*, when the interview results in allowance of the application, by incorporating a complete record of the interview *in an examiner's amendment*." (emphasis added)). Accordingly, I rely on the contents of the Examiner's Amendment to ascertain what was discussed in the interview.

Finally, I am not persuaded by Amgen's argument that the Examiner's Amendment was a clarifying amendment, because the cases on which Amgen relies to illustrate its position are inapposite. (D.I. 359 at 55-58). In those cases, the "clarifying" amendments did not lead to prosecution history estoppel, because the first prong of the *Festo* test was not satisfied: the amendment did not narrow the claims. *See, e.g.*, *Intendis GMBH v. Glenmark Pharma. Inc., USA*, 822 F.3d 1355, 1365 (Fed. Cir. 2016) ("Amendment-based estoppel does not apply because the amendment was not a narrowing amendment made to obtain the patent. Rather, this record demonstrates that the amendment to the dependent claims was a clarifying amendment."); *Interactive Pictures Corp. v. Infinite Pictures, Inc*., 274 F.3d 1371, 1377 (Fed. Cir. 2001) ("As to the amendment-based estoppel issue, we conclude that the addition of the words 'transform calculation' was not a narrowing amendment because that addition did nothing more than make express what had been implicit in the claim as originally worded."); *TurboCare Div. of Demag Delaval Turbomachinery Corp. v. Gen. Elec. Co*., 264 F.3d 1111, 1126 (Fed. Cir. 2001) ("Here, the newly added claim only redefined the small clearance position limitation without narrowing the claim. Therefore *Festo* is not applicable."). If anything, these cases suggest that a clarifying amendment is one that by its nature adds additional language without narrowing a claim. Here, the Examiner's Amendment admittedly narrowed the claims, so it is not a clarifying amendment.

2. Scope of Equivalents Surrendered

Because the Examiner's Amendment narrowed the claims and the amendment was made for substantial reasons related to patentability, a presumption arises that Amgen surrendered all equivalents in "the territory between the original claim and the amended claim." *Festo Corp*., 535 U.S. at 740. Amgen may rebut that presumption by showing that the alleged equivalent (1) "could not reasonably have been described at the time the amendment was made," (2) "was

tangential to the purpose of the amendment," or (3) "was not foreseeable (and thus not claimable) at the time of the amendment." *Research Plastics, Inc. v. Fed. Packaging Corp.*, 421 F.3d 1290, 1298 (Fed. Cir. 2005). Amgen argues that "the tangentiality exception to prosecution history estoppel applies." (D.I. 359 at 66-67).

Amgen has failed to show that the Examiner's Amendment bore no more than a tangential relation to the equivalent in question. "Although there is no hard-and-fast test for what is and what is not a tangential relation, it is clear that an amendment made to avoid prior art that contains the equivalent in question is not tangential." *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1291 (Fed. Cir. 2010). Here, the Examiner's Amendment was able to overcome the prior art by claiming a smaller set of the binders disclosed in the prior art. By agreeing to the Examiner's Amendment, Amgen abandoned the other binders disclosed in the prior art. As the Examiner noted in making his rejection, one of the binders disclosed in both Creekmore and Hsu was "starch." (JTX 5 at SENS-AMG at 295). In fact, Hsu states, "[p]referrably the binder is starch." (PTX 11 at ¶ 46). In this litigation, Amgen has treated the term "starch" as encompassing "pregelatinized starch." Even if Amgen had not done so, Creekmore discloses as a binder the use of "modified starch," which includes pregelatinized starch. (PTX 7 at 2:32-43). The '405 patent does not claim starch or pregelatinized starch as a binder. As a result, prosecution history estoppel bars Amgen from asserting the doctrine of equivalents against Piramal to reclaim pregelatinized starch, or any portion thereof, as a binder. Because Amgen cannot assert the doctrine of equivalents against the binder in Piramal's ANDA product, Amgen cannot prove that Piramal's product infringes claim 1 of the '405 patent.

Finally, all other defendants against whom the doctrine of equivalents was asserted have, like Piramal, raised the defense of prosecution history estoppel. Nevertheless, I have decided for

the sake of expediency to only address the issue as it relates to Piramal.[12] I do not decide, however, that the estoppel defense was not available to these other defendants. Rather, I conclude that even if it was not available, Amgen still could not prove infringement for the reasons stated. In other words, I have not decided the full scope of what Amgen surrendered through prosecution history estoppel, only that it surrendered as an equivalent the use of pregelatinized starch, in whole or in part, as a binder.

3. Conclusion

For the foregoing reasons, Amgen cannot prove that Piramal's product infringes claim 1 of the '405 patent. Per the parties' stipulation, Piramal also does not infringe claims 2-4, 8-17, and 19-20. Finally, under *Wahpeton Canvas*, one who does not infringe an independent claim cannot infringe the dependent claims. 870 F.2d at 1552 n. 9. Therefore, Piramal does not infringe the dependent claims not covered by the stipulation, which are claims 5, 6, and 18.

E. Zydus

Zydus filed Abbreviated New Drug Application No. 20-8971 ("ANDA") with the FDA, seeking approval to market a generic version of cinacalcet hydrochloride in 30, 60, and 90 mg dosage strengths. (D.I. 293, Ex. 1 at ¶ 110). Zydus included a Paragraph IV Certification in its ANDA stating that the '405 patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Zydus' product. (*Id*. at ¶ 111). Amgen, however, claims that Zydus' product will infringe claims 1-4, 6, 8-9, and 15-20 of the '405 patent. (D.I. 293, Ex. 2 at ¶¶ 41-42). Zydus has stipulated that if its ANDA product infringes claim 1, then its ANDA product will also infringe claims 2-4, 8-9, 15-17, and 19 to the extent each claim is found

[12] Amgen has repeatedly indicated that expediency in rendering a decision is important in order to avoid preliminary injunction proceedings. (*See, e.g.*, D.I. 322 at 21:12-16). Only one of the defendants is currently subject to the 30-month stay and Amgen's patent on the active drug cinacalcet HCI expired in March. (*Id*. at 17:22-18:24; 20:8-20).

valid and enforceable. (D.I. 336 at ¶ 5). The stipulation did not cover the asserted claims 6, 18, and 20.

According to the ANDA, Zydus' product has the following composition:

Ingredient	**Function**
Cinacalcet HCl	Active Ingredient
Microcrystalline Cellulose, NF	Diluent
Pregelatinized Starch, NF	Diluent
Hydroxy Propyl Cellulose, NF	Binder
Crospovidone, NF	Disintegrant

(PTX 395 at 27).

Amgen's dispute with Zydus comes down to the function of pregelatinized starch. Amgen takes the position that it functions as a diluent, as stated in Zydus' ANDA. (D.I. 367 at 11). Zydus takes the position that it functions as a binder. (D.I. 360 at 63). Zydus' position adopts an opinion Amgen's expert has asserted against other defendants. (*Id*. at 63-64). Thus, we are in a counterintuitive world where Amgen wins against Zydus only if the opinion of Amgen's expert—which Amgen relies on to prove infringement against the other defendants—is unpersuasive.

1. The Function of Pregelatinized Starch

In tablet formulations, pregelatinized starch can, depending on the context, function as a diluent, binder, or disintegrant. (PTX 438 at 691; PTX 439 at 62). The '405 patent, however,

limited itself by claiming pregelatinized starch only as a diluent.[13] (JTX 2 at 13:21-24). Where a defendant used pregelatinized starch as a binder (like Piramal), or had no binder but used pregelatinized starch as a diluent (like Aurobindo), Amgen's expert, Dr. Davies, opined that pregelatinized starch had two components: a cold water soluble fraction that functioned as a binder and a native starch fraction that functioned as a diluent. (PTX 494 at PIR 229; D.I. 353 at 220:4-221:5; PTX 199 at 30; D.I. 354 at 250:13-251:10). Neither pregelatinized starch nor its cold water soluble fraction are listed in the Markush group for binders. Under my claim construction order, there is no literal infringement if an accused product uses an unlisted binder. (D.I. 300 at 6).

On the face of the ANDA, Zydus' product appears to literally infringe each and every limitation of claim 1. To avoid a finding of literal infringement, Zydus simply adopted Dr. Davies' opinion that the cold water soluble fraction of pregelatinized starch functions as an unlisted binder.[14] (*See* D.I. 354 at 279:7-12). Normally, where literal infringement is unavailable, a patentee can still prove infringement by resorting to the doctrine of equivalents.[15] Here, however, I granted a motion *in limine*, which bars Amgen from asserting the doctrine of equivalents against Zydus. (D.I. 357, D.I. 358). So, if I find Dr. Davies' opinion persuasive, then Amgen cannot prove infringement against Zydus.

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[13] Actually, the '405 patent claims "starch" not "pregelatinized starch" as a diluent. (JTX 2 at 13:21-24). Nevertheless, the parties have litigated the case as if the term "starch" covers pregelatinized starch. (*See* D.I. 294, Ex. 7.1 at 97-99). Thus, for the purposes of this litigation, I read the term "starch" in the '405 patent as covering pregelatinized starch.

[14] Zydus presented its own expert, Dr. Roth, who gave the same opinion as Dr. Davies. (D.I. 356 at 909:18- 912:12). But the only evidence Zydus relied on to corroborate or explain its expert's opinion was Dr. Davies' opinion. (D.I. 360 at 63 (citing Dr. Davies' testimony as evidence for the opinion)). Accordingly, I do not focus on Dr. Roth's duplicative opinion.

[15] With respect to other defendants, Dr. Davies opined that the cold water soluble fraction was equivalent to povidone. (D.I. 353 at 220:20-221:1; D.I. 354 at 257:3-259:1).

Amgen makes no effort to attack the scientific basis for Zydus' argument as doing so would undermine the very infringement theory Amgen asserts against other defendants. (D.I. 359 at 17-18). Nevertheless, for the following reasons, I am not persuaded that Dr. Davies' opinion regarding pregelatinized starch is scientifically sound. To start, Amgen was not consistent in asserting where Dr. Davies' fractions opinion operates, a practice that does not comport with sound scientific principles. Amgen claims that three defendants literally infringe claim 1, because the fractions opinion applies to Aurobindo and Piramal but not to Zydus. But Dr. Davies could not provide a credible explanation for this variation in treatment. (D.I. 354 at 320:1-321:24). First, he said that the pregelatinized starch in Zydus' product functioned only as a diluent, because that was how Zydus identified the pregelatinized starch in its ANDA. (*Id*.). When it was pointed out that Dr. Davies did not accept how pregelatinized starch was identified in other defendants' ANDAs, he agreed and said that was why he was also asserting his fractions opinion against Zydus. (*Id*.).

This shift in infringement theories does not place Amgen in a better position. The '405 patent limits the weight of binders to "from about 1% to about 5%." (JTX 2 at 13:26-27). As Amgen acknowledges, Zydus already uses 4.98% of hydroxy propyl cellulose as a binder. (PTX 395 at 27). If the cold water soluble fraction in Zydus' product also acts a binder, then that is another 3.97% acting as a binder.[16] Adding 4.98% of hydroxy propyl cellulose to 3.97% of a cold water soluble fraction results in a total 8.95% of binder, which exceeds the "about 5%" weight limitation in the '405 patent. (D.I. 355 at 535:15-22). When Zydus raised this point with Dr. Davies, he shifted infringement theories yet again, stating that Zydus' product literally

[16] Zydus product has 11% of pregelatinized starch. (PTX 395 at 27). Dr. Davies claims that 13.1% of pregelatinized starch is a cold water soluble portion. (D.I. 354 at 253:17-254:20; PTX 202). Therefore, 13.1% x 11% = 3.97%

infringed the binder limitation, because there was "at least one" binder from the Markush group in Zydus' product that was within the about 1% to about 5% weight limitation: the 4.98% of hydroxy propyl cellulose. (*Id*. at 539:4-540:12). This testimony is not consistent with the court's controlling claim construction. (*See* D.I. 300; D.I. 357).

The same problems with Dr. Davies' fractions opinion appeared again when Amgen tried to apply it to the pregelatinized starch in the Example of the '405 patent. Dr. Davies claimed that the cold water soluble fraction of the pregelatinized starch in the Example functions as a binder. (D.I. 354 at 315:22-316:11). The Example has 33.378% of pregelatinized starch, of which 4.373% purportedly acts as a binder.[17] (JTX 2 at 11:22-23). Dr. Davies further testified that the 2.044% of povidone in the Example also functions as a binder. (*Id*. at 315:8-13). Adding these two binder amounts together (4.373% of a cold water soluble fraction and 2.044% of povidone) results in 6.417% of binder total. Thus, under Dr. Davies' fractions opinion, the Example would not meet the "from about 1% to about 5%" weight limitation for binders. This issue is avoided, however, if the court adopts Dr. Davies' prior testimony that the pregelatinized starch in the Example is acting only as a diluent. (D.I. 354 at 312:3-23).

The only evidence Amgen presented to corroborate Dr. Davies' fractions opinion is unpersuasive. Amgen relies on a single sentence in the Handbook of Pharmaceutical Granulation Technology stating: "The water-soluble fraction [of pregelatinized starch] acts as a binder, whereas the remaining fraction facilitates the tablet disintegration process." (PTX 439 at 62; D.I. 359 at 19; D.I. 354 at 471:22-472:12). Reading this sentence in the context of the Handbook and the record as a whole, it appears that Amgen imparts too much meaning to the

[17] As stated previously, Dr. Davies claims that 13.1% of pregelatinized starch is a cold water soluble portion. (D.I. 354 at 253:17-254:20; PTX 202). Therefore, 13.1% x 33.378% = 4.373%.

word "acts" in the phrase "acts as a binder." Nowhere else besides that one word does the Handbooks itself or any other scientific literature in the record suggest that only the cold water soluble fraction of pregelatinized starch is acting as the binder. As Aurobindo's expert pointed out, when that same Handbook advises the percentage amount of binders to use in a formula, it advises using 2-5% of "pregelatinized starch," not 2-5% of "the cold water soluble fraction of pregelatinized starch." (PTX 439 at 61; D.I. 356 at 962:3-963:10). If anything, the sentence on which Amgen relies can be reasonably construed to mean that the cold water soluble fraction of pregelatinized starch imparts properties that improve its binding capabilities. The sentence itself makes this suggestion when it addresses the water soluble fraction and the remaining native starch fraction in parallel: It states that the water soluble fraction "acts" as a binder, and the native starch fraction "facilitates" the disintegration process. (PTX 439 at 62). "Facilitates" means "[t]o make easy or easier." Am. Heritage Dictionary (4th ed. 2009).

Ultimately, Dr. Davies consistently asserted, and other experts agreed, that the particular function of pregelatinized starch in any given formulation "depends on the context," including the amount of pregelatinized starch, the other excipients present, and the manufacturing process. (D.I. 354 at 268:21-269:3; *Id*. at 309:21-22; D.I. 355 at 506:15-507:17; *Id*. at 510:2-11; *Id*. at 511:4-512:5). And yet Amgen did not have its expert give testimony that applied those same contextual factors to each specific defendant. On the defense side, however, Aurobindo's expert, Dr. Fassihi, credibly explained how the amount of pregelatinized starch in a particular formulation will dictate its function.[18] (D.I. 356 at 955:21-960:1). As Dr. Fassihi explained and scientific literature confirmed, the theory of percolation holds that when pregelatinized starch is

[18] Similarly, Amneal's expert, Dr. McConville, explained how the manufacturing process affected the function of the pregelatinized starch in Amneal's product. *See*, *supra*, Section III(B)(2).

included in a wet granulation formulation in an amount in excess of about 20% by weight, the pregelatinized starch functions as a diluent. (*Id*. at 961:11-18; DTX 228 at 112-14). When, however, the pregelatinized starch in a wet granulation formulation is between 5% and 10%, the pregelatinized starch functions as a tablet binder. (PTX 438 at 692; *see also* PTX 454 at 408 ("[S]olution binders … are included in the formulation at relatively low concentrations, typically 2-10% by weight.")). When evaluating the ANDA products for Amneal, Piramal, and Zydus, the percolation theory provides the consistency lacking in Dr. Davies' opinion. For example, Amneal and Zydus use over 20% by weight of pregelatinized starch which is consistent with the diluent function identified in their ANDAs. (PTX 183 at 42; PTX 395 at 27). Piramal uses 11% of pregelatinized starch which is consistent with the binder function identified in its ANDA. (PTX 494 at PIR 229). Finally, the Example uses 33.378% of pregelatinized starch which is consistent with a diluent function that would result in the '405 patent covering the Example. (JTX 2 at 11:22-23).

Given all of the foregoing, I find that Amgen has not proven by a preponderance of the evidence that pregelatinized starch should be artificially divided into two fractions, with each fraction alone serving a different function. As a result, Zydus cannot defeat Amgen's assertions of literal infringement by adopting Dr. Davies' opinion that the cold water soluble fraction of pregelatinized starch functions as a binder. Zydus' ANDA product literally infringes claim 1 to the extent the claim is found valid and enforceable.

2. Conclusion

Amgen has asserted claims 1-4, 6, 8-9 and 15-20 of the '405 patent against Zydus. (D.I. 293, Ex. 2 at ¶¶ 41-42). Because I found above that Zydus' ANDA product literally infringes claim 1, I also find per the parties' stipulation that Zydus' ANDA product literally infringes

claims 2-4, 8-9, 15-17, and 19, to the extent each claim is found valid and enforceable. (D.I. 336 at ¶ 5). This leaves for resolution claims 6, 18, and 20. Amgen argues that the use of crospovidone in Zydus' ANDA product literally satisfies claim 6. (D.I. 359 at 16 n. 8). I agree, but only to the extent the claim is found valid and enforceable. Finally, Amgen had the burden to prove by a preponderance of the evidence that Zydus infringed asserted claims 18 and 20, yet for reasons unknown to the court, Amgen neither presented argument on these claims nor entered into a stipulation covering these claims. Accordingly, Amgen has not carried its burden as to claims 18 and 20.

IV. CONCLUSION

For the foregoing reasons, I find that Amgen has not proven infringement as to Amneal, Watson, and Piramal. As to Zydus, Amgen has proven infringement of claims 1-4, 6, 8-9, 15-17, and 19 to the extent the claims are valid and enforceable, but Amgen has not proven infringement of claims 18 and 20. Currently pending before the court is Amneal's motion pursuant to Fed. R. Civ. P. 52(c) for judgment and Zydus' motion pursuant to the same rule for partial judgment. (D.I. 325, D.I. 337). A decision on those motions will be forthcoming.