UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 12-60862-CIV-MIDDLEBROOKS/BRANNON

SHIRE DEVELOPMENT LLC, *et al.*,

Plaintiffs,

vs.

WATSON PHARMACEUTICALS, INC., *et al.*,

Defendants.
_____/

OPINION AND ORDER

THIS CAUSE comes before the Court for final disposition of the issues presented during a bench trial held from April 8, 2013, through April 12, 2013, with closing arguments held on April 26, 2013. Plaintiffs[1] (collectively, "Plaintiffs" or "Shire") assert that Defendants[2] (collectively, "Defendants" or "Watson") infringe Claims 1 and 3 of United States Patent 6,773,720 (the "'720 Patent"). Defendant Watson Florida counterclaims for a declaration that their product does not infringe the '720 Patent, as well as a declaration that the '720 Patent is invalid under 35 U.S.C. § 112(a), for lack of written description and enablement.

[1]"Plaintiffs" refers to: Shire Development LLC ("Shire Development"); Shire Pharmaceutical Development, Inc.; Cosmo Technologies Limited ("Cosmo"); and Giuliani International Limited.

[2]"Defendants" refers to: Actavis, Inc. ("Actavis") (formerly Watson Pharmaceuticals, Inc.); Watson Laboratories, Inc. – Florida ("Watson Florida"); Watson Pharma, Inc. ("Watson Pharma"); and Watson Laboratories, Inc. ("Watson Laboratories"). Watson Florida, Watson Pharma, and Watson Laboratories are wholly owned subsidiaries of Actavis.

This Opinion constitutes the Court's findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52(a). All proposed findings of fact and conclusions of law inconsistent with those set forth herein are rejected.

I. BACKGROUND

The '720 Patent is listed in the FDA's publication titled "Approved Drug Products with Therapeutic Equivalence Evaluations" (commonly known as the "Orange Book") as covering Lialda®. Shire Development is the owner of New Drug Application ("NDA") No. 22000, and is FDA-approved for the manufacture and sale of mesalamine delayed-release tablets containing 1.2 g mesalamine, which are commercialized under the tradename Lialda®. Lialda® is indicated for the induction of remission in adults with active, mild-to-moderate ulcerative colitis and for the maintenance of remission of ulcerative colitis.

On May 8, 2012, Plaintiffs filed this action for infringement of the '720 Patent against Defendants under the Hatch-Waxman Act (the "Hatch-Waxman Act" or the "Act"), 35 U.S.C. § 271.[3]

The Hatch-Waxman Act permits a generic drug manufacturer to obtain approval to market a generic version of a previously approved pharmaceutical product without conducting expensive and time-consuming tests to establish the safety and effectiveness of that product. In place of these safety and efficacy tests, the generic manufacturer must submit an Abbreviated New Drug

[3]It is undisputed that the '720 Patent was issued by the United States Patent and Trademark Office ("USPTO") on August 10, 2004, to Roberto Villa, Massimo Pedrani, Mauro Ajani, and Lorenzo Fossati. They then assigned the '720 Patent to Cosmo S.p.A., which granted an exclusive license to Giuliani S.p.A. Giuliani S.p.A., in turn, granted Plaintiff Shire Pharmaceutical Development Inc. an exclusive sublicense for the '720 Patent. Subsequently, Giuliani S.p.A. assigned the license agreement with Sire Pharmaceutical Development Inc. to Plaintiff Giuliani International Limited. Plaintiff Cosmo Technologies Limited became the owner of the '720 Patent on assignment from Cosmo S.p.A.

Application ("ANDA") to the Federal Drug Administration ("FDA") and demonstrate that its product is bioequivalent to the branded product. 21 U.S.C. § 355(j)(2)(A)(iv). The Hatch-Waxman Act requires that an ANDA applicant submit a "Paragraph IV" certification in its ANDA that the product it seeks FDA approval to market will not infringe any valid U.S. patent. *Id.* § 355(j)(2)(A)(vii)(IV). The Act also requires that an ANDA applicant submit a detailed notice to the patent owner explaining the factual and legal basis for the opinion that the patent is invalid or that the generic product will not infringe the patent. *Id.* § 355(j)(2)(B); *see also* 21 C.F.R. § 314.95(c)(6). The patent owner may file a suit for patent infringement within forty-five days of receipt of a Paragraph IV notice. If the owner files suit, then the FDA may not approve the ANDA for thirty months or until a United States court finds for the defendant based on non-infringement, patent invalidity, or patent unenforceability. *Id.* § 355(j)(5)(B)(iii).

Defendant Watson Florida submitted Watson's ANDA number 203817 ("ANDA Product") to the FDA seeking approval to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of Watson's ANDA Product. Watson's ANDA Product is a generic mesalamine delayed-release tablet and contains 1.2 g mesalamine as the active ingredient.

Watson's ANDA included a "Paragraph IV" certification seeking FDA approval before the expiration of the '720 Patent. On March 26, 2012, pursuant to 21 U.S.C. § 355(j)(2)(B)(iv), Watson sent the Paragraph IV certification to Cosmo Technologies Limited, Young & Thompson, Shire US Inc., and "Shire." Watson's notice indicates that Watson Florida seeks FDA approval to market Watson's ANDA Product before the '720 Patent expires.

Plaintiffs filed their Complaint against Defendants on May 8, 2012, within forty-five days of receipt of the Paragraph IV notice letters, and filed an Amended Complaint (DE 43) on August

3, 2012. Plaintiffs allege infringement of one or more claims of the '720 Patent against all Defendants (Count I), and induced and/or contributory infringement of the '720 Patent by Watson Pharmaceuticals (now Actavis) (Count II). With regard to Count II, Plaintiffs allege that Watson Pharmaceuticals knowingly induced Watson Pharma, Watson Laboratories, and/or Watson Florida to infringe and/or contributed to Watson Pharma's, Watson Laboratories', and/or Watson Florida's infringement of the '720 Patent. They also allege that Watson Pharmaceuticals actively induced, encouraged, aided, or abetted Watson Pharma's, Watson Laboratories', and/or Watson Florida's preparation, submission, and filing of Watson's ANDA with a paragraph IV certification to the '720 Patent. Plaintiffs assert that these acts constitute infringement under 35 U.S.C. § 271.

On August 23, 2012, Defendants filed their Answer (DE 52). Within the Answer, Watson Florida asserts two counterclaims for declaratory relief: (1) a declaration that their ANDA product would not infringe any claim of the '720 Patent, (*see* DE 52 at 15-16); and (2) a declaration that the '720 Patent and its claims are invalid under 35 U.S.C. § 112, for lack of written description and lack of enablement, to the extent the claims are alleged to cover any products set forth in the Watson ANDA. (*See* DE 52 at 16-17).

Plaintiffs are asserting infringement of only Claims 1 and 3 of the '720 Patent. Claim 1 is the Patent's only independent claim, and provides:

> 1. Controlled-release oral pharmaceutical compositions containing as an active ingredient 5-amino-salicylic acid, comprising:
>
> a. an inner lipophilic matrix consisting of substances selected from the group consisting of unsaturated and/or hydrogenated fatty acid, salts, esters or amides thereof, fatty acid mono-, di- or triglycerids, waxes, ceramides, and cholesterol derivatives with melting points below 90° C[], and wherein the active ingredient is dispersed both in said the lipophilic matrix and in the hydrophilic matrix;

b. an outer hydrophilic matrix wherein the lipophilic matrix is dispersed, and said outer hydrophilic matrix consists of compounds selected from the group consisting of polymers or copolymers of acrylic or methacrylic acid, alkylvinyl polymers, hydroxyalkyl celluloses, carboxyalkyl celluloses, polysaccharides, dextrins, pectins, starches and derivatives, alginic acid, and natural or synthetic gums;

c. optionally other excipients;

wherein the active ingredient is present in an amount of 80 to 95% by weight of the total composition, and wherein the active ingredient is dispersed both in the lipophilic matrix and in the hydrophilic matrix.

(DE 202-1 at 4). Claim 3, which is dependent on Claim 1, provides: "Compositions as claimed in [C]laim 1, in the form of tablets, capsules, mintablets." (*Id.*).[4]

At the request of the Parties, and following claim construction briefing and a *Markman* hearing on December 20, 2012, *see Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995), the Court issued an Order dated January 16, 2013 (DE 147), construing certain disputed claims of the '720 Patent. The Court's claim constructions are as follows:

Disputed Claim Term	**Construction**
"matrix"	a macroscopically homogeneous structure in all its volume
"inner lipophilic matrix"	a matrix including at least one lipophilic excipient, where the matrix is located within one or more other substances
"outer hydrophilic matrix"	a matrix of at least one hydrophilic excipient, where the matrix is located outside the inner lipophilic matrix
"dispersed"	sufficiently mixed to incorporate one substance with another

[4]Because Claim 3 is dependent on Claim 1, it necessarily contains all of the limitations of Claim 1. Thus, Watson's ANDA Product can only infringe Claim 3 if it infringes Claim 1. Said differently, if Defendants' ANDA Product does not infringe Claim 1, it cannot infringe Claim 3.

"wherein mesalamine is incorporated with the lipophilic matrix and the hydrophilic matrix"	wherein mesalamine is sufficiently mixed to incorporate it within both the lipophilic matrix and the hydrophilic matrix
"consisting of substances selected from the group consisting of unsaturated and/or hydrogenated fatty acid, salts, esters or amides thereof, fatty acid mono-, di-, or triglycerids, waxes, ceramides, and cholesterol derivatives with melting points below 90°C"	containing one or more of the following substances, each having melting points below 90°C: unsaturated fatty acid, salt of an unsaturated fatty acid, ester of an unsaturated fatty acid, amide of an unsaturated fatty acid, hydrogenated fatty acid, salt of a hydrogenated fatty acid, ester of a hydrogenated fatty acid, amide of a hydrogenated fatty acid, fatty acid monoglycerid, fatty acid diglycerid, fatty acid triglycerid, wax, ceramide, cholesterol derivative
"selected from the group consisting of"	an exclusionary term specifying that an element contains only what is expressly set forth in a recited list, but does not exclude substances unrelated to, or outside of the context of said element
"melting points"	the range of temperatures at which a solid begins to change from a solid to liquid

(*See* DE 147). Further, the Parties agreed to the following claim term constructions:

Agreed Upon Claim Term	**Construction**
"hydrophilic"	having an affinity to water
"lipophilic"	having a poor affinity towards aqueous fluids
"controlled release oral pharmaceutical composition"	an oral pharmaceutical composition whereby the dissolution of active ingredient is not immediate

(*See* DE 68 at 3).

The Court held a non-jury trial from April 8 through April 12, 2013, with closing arguments conducted on April 26, 2013. The Parties filed post-trial proposed findings of fact and conclusions of law on April 19, 2013. After careful consideration of the pleadings, trial and deposition testimony, exhibits, and other submissions, the Court finds as follows.

II. THE LAW OF INFRINGEMENT

Pursuant to 35 U.S.C. § 271(e)(2), it is an act of infringement

> to submit [an ANDA] for a drug claimed in a patent or the use of which is claimed in a patent . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent . . . before the expiration of such patent.

Id. Within the Hatch-Waxman context, the act of infringement that gives rise to a case or controversy has been noted as "artificial," as the specific infringing composition has not yet been made, used, or sold. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997) (citing *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 675, 677 (1990)). In these cases, "[t]he relevant inquiry is whether the patentee has proven by a preponderance of the evidence that the alleged infringer will likely market an infringing product." *Id.* at 1570. That said, "[w]hat is likely to be sold, or, preferably, what will be sold, will ultimately determine whether infringement exists." *Id.*

"Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). Additionally, 35 U.S.C. § 271(c) provides for contributory infringement.

Patent infringement is a question of fact, and a patent is infringed if a single claim is infringed. *Cephalon, Inc. v. Watson Pharms., Inc.*, 707 F.3d 1330, 1340, (Fed. Cir. 2013); *Intervet Am., Inc. v. Kee-Vet Labs., Inc.*, 887 F.2d 1050, 1055 (Fed. Cir. 1989). It is well established that the infringement analysis involves two steps. "First, the court determines the scope and meaning of the patent claims asserted . . . and then the properly construed claims are compared to the allegedly infringing device." *Cybor Corp. v. FAS Techs., Inc.*, 138 F.2d 1448, 1454 (Fed. Cir. 1998). "To prevail, the plaintiff must establish by a preponderance of the evidence that the accused device infringes one or more claims of the patent either literally or under the doctrine of equivalents." *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1247

(Fed. Cir. 2000) (citing *Insituform Techs., Inc. v. Car Contracting, Inc.*, 161 F.3d 668, 692 (Fed. Cir. 1998)).

A. Literal Infringement

"To prove literal infringement, a plaintiff must show that the accused device contains each and every limitation of the asserted claims." *Presidio Components, Inc. v. Am. Technical Ceramics Corp.*, 702 F.3d 1351, 1358 (Fed. Cir. 2012) (citing *Uniloc USA, Inc. v. Microsoft Corp.*, 632 F.3d 1292, 1301 (Fed. Cir. 2011)). This may be done with direct or circumstantial evidence, and a patentee need not present direct evidence of infringement. *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co., Ltd.*, 449 F. App'x 923, 928 (Fed. Cir. 2011) (citing *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1318 (Fed. Cir. 2009); *Symantec Corp. v. Computer Assocs. Int'l, Inc.*, 522 F.3d 1279, 1293 (Fed. Cir. 2008)). Further, it is improper to compare the accused product with a preferred embodiment in the Examples of the patent, instead of with the claims. *See SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985) (citations omitted). "If any claim limitation is absent from the accused device, there is no literal infringement as a matter of law." *Id.* (quoting *Bayer AG*, 212 F.3d at 1247).

B. The Doctrine of Equivalents

An accused product that does not literally infringe a claim may still infringe under the doctrine of equivalents if each limitation of the claim is met in the accused product either literally or equivalently. *Cyber Corp.*, 138 F.3d at 1459 (citations omitted). "The doctrine of equivalents allows the patentee to claim those insubstantial alterations that were not captured in drafting the original patent claim but which could be created through trivial changes." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722, 733 (2002).

To find infringement under the doctrine of equivalents, there must be "a showing that the difference between the claimed invention and the accused product was insubstantial." *Crown Packaging Tech., Inc. v. Rexam Beverage Can Co.*, 559 F.3d 1308, 1312 (Fed. Cir. 2009) (citation omitted). A plaintiff may do so "by showing on a limitation by limitation basis that the accused product performs substantially the same function in substantially the same way with substantially the same result as each claim limitation of the patented product." *Id.* (citing *Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 39-40 (1997)). Indeed, infringement may exist under this doctrine where similar chemicals are used to achieve similar results. *See Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1579-80 (Fed. Cir. 1984); *Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 631 F. Supp. 2d 1010, 1041 (N.D. Ill. 2009); *Glaxo Wellcome, Inc. v. Pharmadyne Corp.*, 32 F. Supp. 2d 265, 291 (D. Md. 1998) ("The use of chemical substitutes for patented ingredients that are from the same family of chemicals may constitute infringement under the doctrine of equivalents.").

III. INFRINGEMENT ANALYSIS

Before analyzing the '720 Patent's claim limitations and the Watson ANDA's relation thereto, it is helpful to first briefly discuss the general nature of mesalamine (the '720 Patent's active ingredient), the Watson ANDA Product, and the Watson's manufacturing process.[5]

A. Mesalamine

The '720 Patent is titled "Mesalazine Controlled Release Oral Pharmaceutical Compositions." The active ingredient in the '720 Patent, as well as in both Lialda® and the

[5] The Court's infringement analysis will focus on Claim 1, since Claim 3 is dependent on Claim 1, and it appears to be undisputed that the Watson ANDA Product infringes Claim 3.

Watson ANDA Product, is mesalamine. (DE 202-1 at 6). Mesalamine is also known as 5-amino-salicylic acid and mesalazine. (*Id.* at ¶ 33).

Mesalamine is a locally acting drug, and high amounts of it are required to treat ulcerative colitis. (Trial Tr. Day 1 at 55:12-20 and 58:25 to 59:8 (Streck Direct); Trial Tr. Day 2 at 71:20-23 (Joshi Dep.)). This in turn requires that oral tablet formulations have high dosages and percentages of mesalamine. (Trial Tr. Day 1 at 58:25 to 59:16 (Streck Direct); Trial Tr. Day 3 at 232:6-10 (Sinko Cross)).

Because mesalamine is a locally acting drug, and ulcerative colitis can occur anywhere throughout the colon, it is important for mesalamine to be formulated for release at the beginning of the colon and then continued slow release throughout the length of the colon. If it releases before the colon and is absorbed into the bloodstream, it will not be effective. (Trial Tr. Day 1 at 55:6-9 (Streck Direct); Trial Tr. Day 3 at 194:12 to 195:6 (Sinko Direct)).

B. The Watson ANDA Product and Manufacturing Process

The Watson ANDA Product is a tablet containing mesalamine as an active ingredient, as well as several other non-active ingredients, called "excipients." Mesalamine is present in an amount of 80 to 95% by weight of the total composition. (DE 202-1 at ¶¶ 32-40).

Watson's manufacturing process can be described in five steps: (1) Granulation; (2) Blending; (3) Compression; (4) Coating; and (5) Packaging. (PTX 023 at 87).

"Granulation" is performed by mixing mesalamine in powder form with a filler (microcrystalline cellulose) and a binding solution of povidone and copovidone in ethanol. (PTX 023 at 88; *see also* Trial Tr. Day 3 at 173:25 to 174:5 (Sinko Direct); Trial Tr. Day 4 at 169:25 to

170:2 (Brittain Redirect) and 219:10-16 (Kibbe Direct)).[6] That mixture is then put through a device known as a granulator to produce granules. (PTX 023 at 87, 88). This process is known as "wet granulation." The wet granulation process forms granules of mesalamine and these excipients, as well as other smaller particles called "fines." (PTX 023 at 67-68; Trial Tr. Day 3 at 139:11-18 (Gupta 30-b-6 Dep.)).[7] As the mesalamine granules are dried, the ethanol evaporates, leaving pores in the granules. (Trial Tr. Day 3 at 173:16 to 175:10 (Sinko Direct); Trial Tr. Day 1 at 201:7-12 (Tian Dep.)). These granules are then milled. (PTX 023 at 88; Trial Tr. Day 3 at 173:8-15 (Sinko Direct); Trial Tr. Day 4 at 226:6-25 (Kibbe Direct)).[8] Granulation and milling produce granules of relatively uniform size and, as noted above, also produce fine particles of mesalamine. (Trial Tr. Day 3 at 139:11 to 140:17 (Gupta 30-b-6 Dep.) ("[W]hen we do granulation, wet granulation, we do not get [one] hundred percent granules. We get a lot of fines as well."); Trial Tr. Day 1 at 203:16 to 204:19 (Tian Dep.); Trial Tr. Day 3 at 189:21 to 190:13 (Sinko Direct)). These fines – or small particles – contain mesalamine, the active ingredient. (Trial Tr. Day 3 at 189:6 to 191:20 (Sinko Direct); *see also* Trial Tr. Day 1 at 205:5-7 (Tian Dep.) ("Q: Would the fines that come out of the wet granulation process that you studied contain mesalamine in them? A: Yeah.")).

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[6] According to Watson's Product Development Report, "[a] binder is required during wet granulation to achieve good cohesive granules which possess good flow, and to provide a tablet with adequate crushing strength." (PTX 023 at 24).

[7] The issue of these "fines" will be addressed in more detail below.

[8] According to Dr. Kibbe, the granules have a tendency to "clump up" after or during the drying process. For this reason, the granules are run through a mill, which Dr. Kibbe compares to a "large flour sifter," to break down the granule "clumps." (Trial Tr. Day 4 at 226:6-25 (Kibbe Direct)).

Watson then blends the mixture of granules and fines with magnesium stearate,[9] sodium starch glycolate,[10] and colloidal silicon dioxide. (PTX 023 at 88; *see also* Trial Tr. Day 3 at 174:25 to 175:7 (Sinko Direct)).

After the mixture is blended, it is compressed into tablets. (PTX 023 at 88). The tablets are then coated with an enteric coating and a film coating.[11]

C. The Claim Limitations

Claim 1 of the '720 Patent has several claim limitations, all of which – as discussed above – must be met in order for the Court to make a finding of literal infringement. First, Claim 1 requires "controlled-release oral pharmaceutical compositions" that have 5-amino-salicylic acid (mesalamine) as the active ingredient. Additionally, Claim 1 requires the mesalamine to be present in an amount of 80-95% by weight of the total composition.[12] Next, there must be an "inner lipophilic matrix" that consists of one or more of the listed lipophilic[13] substances. Further, the lipophilic excipients used to form the lipophilic matrix must have a melting point

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[9] Magnesium stearate is lipophilic and is the salt of a hydrogenated fatty acid. (DE 202-1 at ¶ 36; Trial Tr. Day 3 at 169:3-5 and 171:23-25 (Sinko Direct); *see also* Trial Tr. Day 5 at 64:6-20 (Kibbe Cross); Trial Tr. Day 1 at 81:10-14 and 87:11-13 (Bugay Direct); Trial Tr. Day 3 at 132:10-13 and 134:25 to 135:7 (Gupta 30-b-6 Dep.); Trial Tr. Day 2 at 76:13-20 (Joshi Dep.)).

[10] Sodium starch glycolate is a hydrophilic compound and a starch derivative. (DE 202-1 at ¶¶ 38, 39).

[11] Enteric coatings are insoluble at low pH environments (like the stomach) but are soluble in higher pH environments (like the intestines). (Trial Tr. Day 2 at 25:6-25 (Little Direct); PTX 023 at 32). This pH-dependent property is employed to protect the contents of the tablet in the stomach, but will permit release in the intestines. (Trial Tr. Day 2 at 25:6-25 (Little Direct); PTX 023 at 29).

[12] It is undisputed that the Watson ANDA Product is a tablet – or oral pharmaceutical composition – that contains mesalamine as an active ingredient and in an amount of 80 to 95% by weight of the total composition. (DE 202-1 at ¶¶ 34, 40). Accordingly, the Court's analysis will not address these limitations.

[13] As agreed to by the Parties and understood by the Court, the adjective "lipophilic" means "having a poor affinity towards aqueous fluids."

below 90 ° C. Claim 1 also requires an "outer hydrophilic matrix" consisting of one of the listed hydrophilic[14] substances. Finally, Claim 1 requires that mesalamine be dispersed in each of the matrices.

i. "Controlled-Release"

The Parties have agreed that the meaning of "controlled-release oral pharmaceutical compositions" is "an oral pharmaceutical composition whereby the dissolution of active ingredient is not immediate." (DE 68 at 3). The definition of "immediate release" slightly varies between the experts. For example, Plaintiffs' expert, Dr. Sinko, defines an immediate release product as one that releases at least 75% of active ingredient in 45 minutes. (Trial Tr. Day 3 at 193:18-21 (Sinko Direct)). On the other hand, Watson formulator Dr. Joshi describes an immediate release product as one that releases 85% of active ingredient in 30 minutes. (Trial Tr. Day 2 at 73 (Joshi Dep.)).

Defendants argue that Claim 1 requires a controlled-release *core*, and their ANDA Product's core is immediate release. For their finished product's controlled-release characteristics, Defendants blame the tablet's enteric coating.

While the enteric coating does have the effect of delaying release, Plaintiffs offered evidence that the Watson core itself is controlled-release, with the inner and outer matrices working together to delay the release of mesalamine. Plaintiffs provided the Watson Product Development Report (the "Watson PDR"), which indicates that the core of Watson's tablet releases 36% of mesalamine after one hour of residence in pH 7.2 phosphate buffer. (PTX 023 at

[14] As agreed to by the Parties and understood by the Court, the adjective "hydrophilic" means "having an affinity to water."

81).[15] Plaintiffs' expert Dr. Sinko confirmed at trial that the Watson PDR clearly indicates that the Watson ANDA Product's core is not immediate release. The Watson PDR also reports that the core tablet requires seven to nine hours of residence in pH 7.4 Kreb's bicarbonate buffer before releasing 75% mesalamine. (PTX 023 at 82; *see also* Trial Tr. Day 3 at 198:9-14 (Sinko Direct) ("If you look at the first two hours, that's going to be the delayed component. After that, you can see that even hour seven, which is really hour five, you are still not hitting even my conservative threshold for immediate release. It is clearly a controlled release formulation.")).

Plaintiffs also introduced Dr. Steven Little, an expert in controlled release formulation and testing, who conducted enteric coat dissolution-compromise studies of the Watson ANDA Product. Dr. Little conducted experiments to observe the dissolution and removal of the enteric coating for the Watson ANDA Product in a 1 Liter, pH 7.2 phosphate buffer vessel, with stirring comparable to a USP Paddle 2 apparatus.[16] According to Dr. Little, his goal was to observe whether the enteric coating on the Watson ANDA Product would be responsible for the slow, sustained release shown in the Watson PDR. In his experiments, Dr. Little observed that the Watson ANDA Product's enteric coating is ruptured within minutes and is severely compromised within 30 minutes after being exposed to pH 7.2 phosphate buffer.[17] Dr. Little's images show that the enteric coating on the Watson tablet was clearly compromised after ten minutes in pH 7.2. At

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[15] Although the Watson ANDA Product's dissolution profile tests the final product, as opposed to just the core of the tablet, Plaintiffs' expert Dr. Sinko testified that the enteric coating would not come off until hour three of the dissolution testing. Thus, hour four in the dissolution profile is really hour one when determining the dissolution of mesalamine. (*See* Trial Tr. Day 3 at 196:23 to 197:12 (Bugay Direct)).

[16] One of Dr. Little's goals in his study was to approximate the conditions that were used in the Watson PDR for the Watson ANDA. (Trial Tr. Day 2 at 27:8-25 (Little Direct)).

[17] Dr. Little recorded photographic images of the tablet every two minutes using a high resolution camera. These photographs were displayed during the trial.

30 minutes, the coating was extremely compromised, and between 30 and 32 minutes the coating had come off the top of the tablet. Dr. Little also observed that after 32 minutes, when the enteric coating was completely compromised – and the mesalamine was exposed to the buffer solution on all sides – the mesalamine granules from the Watson ANDA Product were not dissolving. Dr. Little provided images of the tablet after 68 minutes, which show what Dr. Little described as "a pile of . . . undissolved mesalamine granules." (Trial Tr. Day 2 at 36:25 to 37:3 (Little Direct); *see also* PTX 222). After 86 minutes, and toward the end of the experiment, Dr. Little's images demonstrate that there is still a pile – albeit a smaller pile – of mesalamine granules resting at the bottom of the vessel. (*See* PTX 231). Based on the very high solubility of mesalamine and his own testing of the Watson ANDA Product, Dr. Little concluded that it was not the enteric coating of the Watson ANDA Product that delayed the release of mesalamine. Rather, Dr. Little found that "there must be something else added in the system that would result in the slower release that is seen." (Trial Tr. Day 2 at 39:22 to 40:2 (Little Direct)).

Having viewed the evidence and listened to the testimony, I find that Plaintiffs have met their burden to prove by a preponderance of the evidence that the Watson ANDA Product is "controlled-release."[18]

ii. "Inner Lipophilic Matrix"

The Court has construed "matrix" to mean "a macroscopically homogeneous structure in all its volume" and "inner lipophilic matrix" to mean "a matrix including at least one lipophilic excipient, where the matrix is located within one or more other substances." (DE 147 at 6-9).

[18] The Court notes that this conclusion stands even as to the core of the Watson ANDA Product.

Plaintiffs contend that the inner lipophilic matrix in the Watson ANDA Product is the macroscopically homogeneous distribution of magnesium stearate[19] itself within the volume defined by the perimeter of the Product's mesalamine granules. In support, Plaintiffs offered the results of several tests conducted by Dr. David Bugay, their analytical chemist with over 25 years of experience in analytical chemistry.

First, Dr. Bugay conducted Scanning Electron Microscopy ("SEM")[20] and Energy Dispersive X-Radiation ("EDX")[21] analysis on the uncoated (or core) tablets used to make the final Watson ANDA Product. In short, the SEM-EDX testing correlates the topographical features of a tablet cross section with the identity and location of magnesium stearate in the same field of view.[22] The images from the testing show magnesium stearate to be evenly distributed throughout the core of the Watson tablet – including within the tablet's mesalamine granules – thereby forming a macroscopically homogeneous structure in all of the volume of the mesalamine granules. Thus, the lipophilic matrix is located within one or more other substances – the

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[19] It is undisputed that the Watson ANDA Product contains magnesium stearate, and that magnesium stearate is lipophilic. Further, experts from both sides testified that magnesium stearate is the salt of a hydrogenated fatty acid – one of the categories of substances listed in the '720 Patent's Claim 1(a). (*See* Trial Tr. Day 3 at 168:12 to 169:5 (Sinko Direct); Trial Tr. Day 5 at 64:12-20 (Kibbe Cross)). Whether magnesium stearate has a melting point below 90° C is a point of contention between the Parties, and will be addressed in detail below.

[20] SEM is a microscopy technique that uses a beam of electrons to obtain an image of a sample's topography, such as the outline of compressed granules in a tablet cross-section. When the beam of electrons impinges on the sample, secondary electrons are emitted and detected to form an image. (Trial Tr. Day 1 at 77:3 to 78:4 (Bugay Direct)). According to Plaintiffs' expert, "[t]his is a very common technique utilized in the pharmaceutical industry." (Trial Tr. Day 1 at 78:3-4 (Bugay Direct)).

[21] EDX is a technique conducted in the same apparatus as SEM, but instead of monitoring secondary electrons, EDX monitors X-rays emitted from elemental nuclei of a sample. The emitted X-rays are unique to each particular element. (Trial Tr. Day 1 at 78:5-21 (Bugay Direct)). SEM coupled with EDX allows for the detection of an element at a location in the sample. (Trial Tr. Day 1 at 78:22 to 80:1 (Bugay Direct)).

[22] This was also done to identify and locate sodium starch glycolate, as discussed below.

mesalamine granules – in accordance with the Court's construction of "inner lipophilic matrix."

While Defendants attempted to cast doubt on the reliability of the SEM-EDX testing done by Dr. Bugay, even implying that his results are "artifacts" of "smearing" from the microtoming process,[23] Defendants offered no expert testimony that Dr. Bugay's results exhibit "striations," "cratering," or "bulldozing" – all of which are classic indicia of "smearing" and are widely recognized by analytical chemists as such. Additionally, Dr. Bugay examined six cross-sectioned surfaces with SEM-EDX (three surfaces from two tablets), with each surface providing similar images. This demonstrates the consistency of the methods.

Defendants also argued that Dr. Bugay's images showing magnesium stearate within the mesalamine granules is inconsistent with the Watson manufacturing process that adds magnesium stearate to the granules *after* the granules are formed. However, as explained by Dr. Sinko, the mesalamine granules have pores, and the magnesium stearate is able to infiltrate the pores of the granules upon tablet compression. (Trial Tr. Day 3 at 173:16 to 175:18 (Sinko Direct); Trial Tr. Day 1 at 201:5-12 (Tian Dep.) ("Q: Would it be fair to say that in your experience all granules will have some pores in them? A: Yes.")).

Another argument by Defendants is that the '720 Patent requires an inner lipophilic matrix that is spatially "separate and distinct" from the outer hydrophilic matrix. Defendants contend that the presence of sodium starch glycolate inside the mesalamine granules and magnesium stearate outside the mesalamine granules means that the Watson ANDA Product contains "mixed

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[23] Microtomy is used for the creation of flat, cross-sectioned surfaces. Dr. Bugay used microtomy to prepare the tablet samples for SEM-EDX analysis. In doing so, Dr. Bugay epoxied each tablet onto a T-mount and positioned a stainless steel blade at a predetermined angle. The tablet is then brought downward across the blade in a repetitive fashion. For the final preparation of each sample, Dr. Bugay employed an extremely sharp, diamond-tipped blade to expose the flattest possible surface for analysis.

matrices," which is outside the scope of the '720 Patent. In support of this argument, Defendants rely on the prosecution history of the '720 Patent and Dr. Kibbe's testimony that the '720 Patent requires "separate and distinct" matrices.

As addressed during claim construction, and demonstrated at trial, the Patent does not require a particular physical or spatial structure with matrices separate and distinct from each other.[24] Rather, what matters is the relationship between the excipients in different locations. As testified to by Dr. Sinko, the terms "inner" and "outer" sufficiently describe the right place in which each matrix must be in order to perform its function and control the release of mesalamine.[25]

Further, Plaintiffs have shown that the Watson ANDA Product's inner lipophilic matrix is the magnesium stearate itself that is dispersed with the mesalamine in the granules. Only the magnesium stearate makes up the inner lipophilic matrix. Plaintiffs have also shown that other chemical substances can be present within the same region as the lipophilic excipients, and that the sodium starch glycolate found within the granules fits within the "optionally other excipients" limitation of Claim 1(c).

After considering the evidence presented and the testimony from both Parties, I find that Plaintiffs have proven by a preponderance of the evidence that the Watson ANDA Product

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[24] As noted in the Court's claim construction Order, "[nowhere] in the prosecution history, claims, or specification does the term 'separate and distinct' appear." (DE 147 at 8).

[25] As explained by Dr. Sinko on cross examination, excipients found in different locations within the tablet will play different roles. For example, the magnesium stearate located in the granules will have an effect on the release of the mesalamine, whereas magnesium stearate in the extragranular space will serve as a lubricant. Similarly, sodium starch glycolate in the extragranular space will affect the release of mesalamine, while sodium starch glycolate within the granules – according to Dr. Sinko – will be irrelevant. (*See* Trial Tr. Day 3 at 232-233). Thus, although these substances are the matrix-forming substances in the tablet, each has different functions depending on its relation to the granules. This also does not violate the "consisting of" limitation, as the sodium starch glycolate within the granules does not form the inner lipophilic matrix and is unrelated to this element of the Claim.

contains an "inner lipophilic matrix" that is "located within one or more other substances," since the lipophilic matrix contained by the granules is located within at least the sodium starch glycolate particles outside the granules. Thus, this aspect of Claim 1 has been met.

iii. "Melting Points Below 90° C"

In order for magnesium stearate to fall within Claim 1(a)'s realm of substances, it must have melting points below 90° C. Establishing the melting points of a substance might seem like an easy concept; however, in this case, the melting points (or the range of temperatures at which a solid begins to turn from a solid to liquid) of magnesium stearate has become hotly contested.

To prove that magnesium stearate has melting points below 90° C, Plaintiffs' expert Dr. Bugay tested the magnesium stearate found in the Watson ANDA Product.[26] Dr. Bugay used infrared spectroscopy to determine that the magnesium stearate provided by Watson is a hydrate of magnesium stearate (also known as "magnesium stearate dihydrate").[27] Plaintiffs also provided the testimony of Dr. Rodolfo Pinal, an expert on the issue of melting points. Dr. Pinal, who I find to be credible, relied on Dr. Bugay's testing results and several past- and present-day references to

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[26] Specifically, Dr. Bugay subjected the Watson magnesium stearate sample to differential scanning calorimetry ("DSC") and thermogravimetric analysis ("TGA"), both of which are forms of thermal analysis. DSC measures heat flow of a sample as it is subjected to a heating profile (e.g., an increase in temperature at a constant rate, such as 10° C per minute, within a temperature tange). If a sample undergoes a thermal transition within that temperature range, heat may flow into or out of the tested sample. A transition where heat flows into the sample is known as an endothermic event. A transition where heat flows out of the sample is known as an exothermic event. An endothermic event is represented by a downward peak on a DSC thermogram. Both melting and dehydration are endothermic events.

TGA measures weight loss or gain from a sample as it is subjected to heating. A weight loss may indicate that the material had some residual solvent on its exterior that is given off, or, in the case of a hydrate, a weight loss may also indicate the evolution of the water-of-crystallization from a sample.

[27] Magnesium stearate can exist in different forms, such as "dihydrate" and "anhydrate," indicating the presence of water molecules.

conclude that the magnesium stearate used in the Watson ANDA Product has a melting point below 90° C. Dr. Pinal also relied on the website of Watson's magnesium stearate supplier, Covidien/Mallinckrodt, which reports magnesium stearate to have a melting point below 90° C.

Defendants provided its own expert in the field, Dr. Harry Brittain, who relied on his own references, as well as Dr. Bugay's test results, to support Watson's argument that magnesium stearate does not melt until a temperature in excess of 100° C.

Dr. Bugay's testing demonstrates two endothermic events: one around 80° C, another around 125° C. There is no dispute that the second endothermic peak (going from low to high temperature) is a melt of the anhydrous form of magnesium stearate.[28] However, it is the first peak, beginning below 90° C, on which the experts butt heads. Plaintiffs' expert claims that the first peak is the simultaneous dehydration *and* melt of magnesium stearate dihydrate. Thus, according to Dr. Pinal, the magnesium stearate used in the Watson ANDA Product (the dihydrate form) has a melting point below 90° C. Dr. Brittain, on the other hand, claims that the first peak is *only* the dehydration of magnesium stearate, and thus magnesium stearate "melts" at the second endothermic event, when the temperature is above 90° C and magnesium stearate is dehydrated.[29]

Considering the different expert opinions and the evidence presented, I find that Plaintiffs have proven by a preponderance of the evidence that magnesium stearate dihydrate – the substance used in the Watson ANDA Product – melts below 90° C. In making this determination, I found Dr. Pinal's analysis very credible. Specifically, Dr. Pinal explained that the second endothermic

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[28] The hydrated form of magnesium stearate is a crystalline structure where water forms part of the crystal lattice structure. The dehydrated form of magnesium stearate is also a crystalline structure; however, it does not have water molecules.

[29] Dr. Brittain opined that hydrates could not simultaneously dehydrate and melt. However, Dr. Brittain did not refer to any literature in arriving at this opinion, and Plaintiffs were able to point to a reference that contradicted this absolute opinion.

peak in Dr. Bugay's testing shows a very sharp peak that is the melt from a pure, high quality crystal. This is important because it demonstrates what happened during the first peak. Dr. Pinal opined that such a high quality crystal needs to be produced from a liquid, and since that liquid would have to be created during the first endothermic peak, the crystalline magnesium stearate dihydrate must turn from solid to liquid during the first peak. Dr. Pinal also relied on two literature references that reported a loss of anisotropy[30] accompanying the first endotherm of the DSC for magnesium stearate. This bolstered his opinion that the dehydration of magnesium stearate at the first endothermic peak was accompanied by a melt.

I also acknowledge that many present-day references indicate that magnesium stearate has a melting point far above 90° C. However, it was clear from the testimony that these melting points are those of the anhydrous form of magnesium stearate, which is not used in the Watson ANDA Product. While the experts were inconclusive as to why some references – namely, the Handbook of Pharmaceutical Excipients – changed the melting point of magnesium stearate to the higher, anhydrous form melting points in recent editions, this is of little consequence to the Court, as Plaintiffs have shown by a preponderance of the evidence that the hydrated form of magnesium stearate found in the Watson ANDA Product begins to turn to liquid at the first endothermic peak.

a. Doctrine of Equivalents

Even if the melting point of magnesium stearate were found to be above 90° C, the doctrine of equivalents would nevertheless require a finding of infringement. Specifically, magnesium stearate is equivalent to stearic acid, which is lipophilic and a hydrogenated fatty acid that has a

[30] Anisotropy is a property of crystals when studied under polarized light. The loss of anisotropy is associated with the loss of crystallinity. The loss of crystallinity is also consistent with a melt, or the formation of a liquid.

melting point below 90° C. Plaintiffs' experts testified not only that magnesium stearate and stearic acid are "related compounds," but also that they both are known to perform the function of slowing drug release by virtue of their lipophilic nature. In fact, Dr. Sinko testified that using stearic acid in the '720 Patent and using magnesium stearate in the Watson ANDA Product has the same result: it would control the release of mesalamine. (Trial Tr. Day 3 at 205:13-19 (Sinko Direct)).[31] In essence, Plaintiffs have shown that the use of magnesium stearate in the Watson ANDA Product performs substantially the same function in substantially the same way with substantially the same result as the use of stearic acid with a melting point below 90° C. *See Crown Packaging*, 559 F.3d at 1312.

Accordingly, I find that Plaintiffs' have met their burden to show that, under the doctrine of equivalents, the Watson ANDA Product meets Claim 1's requirement of a listed lipophilic excipient with a melting point below 90° C.[32]

iv. "Outer Hydrophilic Matrix"

The Court has construed the term "outer hydrophilic matrix" to mean "a matrix of at least one hydrophilic excipient, where the matrix is located outside the inner lipophilic matrix."[33]

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[31] Dr. Sinko's conclusion that the magnesium stearate in the Watson ANDA Product retards the release of mesalamine is based on the testing and testimony of Shire's expert, Dr. Little, the deposition of Dr. Joshi, a Watson formulator, and the testing and opinion of Dr. Lee Trevino, an expert for Defendants who tested the dissolution properties of Watson's milled mesalamine granules. (*See* Trial Tr. Day 3 at 205:20 to 206:18 (Sinko Direct)).

[32] Defendants argue that applying the doctrine of equivalents will vitiate an entire claim limitation – that the lipophilic excipients have melting points below 90° C. However, under the totality of the circumstances, I find that the "all limitations rule" does not preempt application of the doctrine. Notably, stearic acid and magnesium stearate would have the same function in the product, and magnesium stearate undergoes a change below 90° C. Whether this is called a melt or a dehydration (or both), swapping the two chemicals in the formulation would be an insubstantial change. *See Pfizer, Inc. v. Teva Pharms., USA, Inc.*, 429 F.3d 1364, 1379-80 (Fed. Cir. 2005) (citations omitted).

It is undisputed that the Watson ANDA Product contains sodium starch glycolate, and that sodium starch glycolate is a starch derivative that fits within the substances listed in Claim 1(b). (*See* DE 202-1 at ¶¶ 37-39). Plaintiffs contend that sodium starch glycolate in the Watson ANDA Product forms a hydrophilic matrix in the extragranular space outside the mesalamine granules, which contain the lipophilic matrix. To Plaintiffs, this satisfies the requirement of Claim 1(b) that the hydrophilic matrix be *outside* the inner lipophilic matrix.

Plaintiffs have supplied ample evidence and testimony to support their position. Specifically, Dr. Bugay's SEM-EDX testing reveals the macroscopically homogeneous distribution of sodium starch glycolate inside and outside the mesalamine granules in Watson's ANDA Product. Moreover, the SEM-EDX overlay images show clusters of sodium starch glycolate in the extragranular space of the Watson tablet. Drs. Bugay and Sinko testified that these aggregates of sodium starch glycolate form the outer hydrophilic matrices in the extragranular space.

Defendants' argument regarding the hydrophilic matrix is similar to their argument regarding the lipophilic matrix: because magnesium stearate – the lipophilic matrix-forming substance – is present in the extragranular space with the sodium starch glycolate, the matrices are mixed, and such dual presence violates the "consisting of" limitation of Claim 1(b). They also claim this renders the "inner" and "outer" matrix requirements meaningless. However, as discussed above, this argument is unavailing, as the matrices need not be "separate and distinct," and the magnesium stearate outside the granules does not form the lipophilic matrix under Claim 1(a). Rather, the magnesium stearate in the extragranular space may have another function (e.g.,

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[33] As noted above, the term "matrix" is construed to mean "a macroscopically homogeneous structure in all its volume."

lubricant) and is unrelated to the formation of the matrices. Similarly, it is the extragranular sodium starch glycolate itself that makes up the outer hydrophilic matrix. This "outer" matrix is not mixing with the inner lipophilic matrix, which is one the magnesium stearate located within the granules.

Heaving considered the evidence and the arguments made by both sides, I find that Plaintiffs have shown by a preponderance of the evidence that Claim 1(b) is infringed by the Watson ANDA Product. Specifically, Plaintiffs have shown that it is more likely than not that the sodium starch glycolate in the Watson ANDA Product forms a hydrophilic matrix that is outside of the mesalamine granules that contain the lipophilic matrix. Thus, the hydrophilic matrix is "outer" with respect to the lipophilic matrix.

v. "Wherein the Active Ingredient is Dispersed Both in the Lipophilic Matrix and in the Hydrophilic Matrix"

The final limitation of Claim 1 is that mesalamine must be dispersed[34] in both lipophilic and hydrophilic matrices. To demonstrate the distribution of mesalamine within the Watson ANDA Product, Dr. Bugay analyzed two of the surfaces he analyzed by SEM and EDX with Raman imaging.[35] Each surface Dr. Bugay analyzed showed mesalamine consistently positioned throughout the entire two-dimensional area of the cross-sectioned surface. In sum, the Raman imaging shows mesalamine dispersed throughout the entire tablet.

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[34] "Dispersed" was construed to mean "sufficiently mixed to incorporate one substance with another." "[W]herein mesalamine is incorporated with the lipophilic matrix and the hydrophilic matrix" was construed to mean "wherein mesalamine is sufficiently mixed to incorporate it within both the lipophilic matrix and the hydrophilic matrix."

[35] Raman imaging is a form of spectroscopy that allows for identification of chemical compounds. Raman spectroscopy measures vibrational frequencies between different atoms, and the frequency of the vibrations depends on the structure of the chemical compound. Coupling Raman spectroscopy with a microscopic imaging technique allows for the determination of the location of a compound of interest – in our case, mesalamine.

As previously discussed, the macroscopically homogeneous distribution of magnesium stearate in the Watson ANDA Product's granules gives rise to an inner lipophilic matrix. Further, it has been shown that mesalamine is sufficiently mixed within the granules.[36] Thus, with regard to the inner lipophilic matrix, Plaintiffs have demonstrated by a preponderance of the evidence that mesalamine is dispersed in the inner lipophilic matrix.

Plaintiffs' expert, Dr. Sinko, relied on Watson's manufacturing process, the testimony of Watson formulators, Messrs. Gupta and Tian, as well as the Raman imaging to conclude that mesalamine is dispersed in the hydrophilic matrix. (*See* Trial Tr. Day 3 at 189:6-15 (Sinko Direct)). Dr. Sinko explained that during the manufacturing process of the Watson ANDA Product, "fines" (or small particles) of mesalamine are created during the granulation process. These "fines" can also be created during the milling step of manufacturing. The mesalamine granules and fines are mixed with other ingredients, including sodium starch glycolate, during the manufacturing process. Plaintiffs contend that these fines are small particles of mesalamine and are outside of the granules in the extragranular space. One of the Watson ANDA Product formulators, Raghavendra Gupta, testified by videotaped deposition that both granules and fines are formed during the granulation step of the manufacturing process.[37] He also testified that "[s]odium starch glycolate, when mixed with the granulation, it would be mixing with the fines also, so it will be going into the whole matrix, which would be the granules and the fines obtained from the granulation." (Trial Tr. Day 3 at 140:7-10 (Gupta 30-b-6 Dep.)).

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[36] The Raman imaging shows the granules to have the highest concentration of mesalamine.

[37] At one point in the testimony, Mr. Gupta explains that "we do not get [one] hundred percent granules. We get a lot of fines as well." (Trial Tr. Day 3 at 139:15-18 (Gupta 30-b-6 Dep.)).

Defendants argue that these "fines" are merely smaller granules, and that there can be no "fines" in the extragranular space because they are themselves granules. (*See* Trial Tr. Day 5 at 101:20-25 (Kibbe Cross)).[38] If the "fines" are granules, then mesalamine cannot be dispersed in the extragranular outer hydrophilic matrix.

Notwithstanding the semantic game of "fine vs. granule," I find that Plaintiffs have the stronger argument and have proven by a preponderance of the evidence that mesalamine is dispersed in the outer hydrophilic matrix. Plaintiffs have met their burden by demonstrating that small particles of mesalamine are in the extragranular space, dispersed with the sodium starch glycolate. Moreover, as testified to by Drs. Bugay and Sinko, this conclusion is supported by the Raman imaging experiment that shows mesalamine uniformly distributed throughout the tablet.[39]

IV. INVALIDITY

As discussed above, Defendant Watson Florida asks the Court to declare that the '720 Patent is invalid under 35 U.S.C. § 112 for lack of written description and/or lack of enablement. Watson Florida argues that if the Watson ANDA Product is found to infringe the '720 Patent, then the Patent is invalid for lack of written description and enablement because the Watson ANDA Product is not adequately described in or enabled by the '720 Patent. Further, Watson Florida argues that if the claims are construed broad enough to encompass the Watson ANDA product, then the '720 Patent's written description is inadequate because it does not teach a "mixed matrix" composition.

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[38] Another Watson employee, Mr. Tian, testified by video deposition that these "fines" are indeed granules. (Trial Tr. Day 204:7-19 (Tian Dep.)). He also testified that these "fines" contain mesalamine in them. (Trial Tr. Day 204:20-22 (Tian Dep.)).

[39] Additionally, Defendants did no testing of their own to show that the "fines" are indeed small granules.

A. Legal Standard

"A party asserting invalidity must present clear and convincing evidence to overcome a patent's presumption of validity." *Pozen Inc. v. Par Pharm., Inc.*, 696 F.3d 1151, 1159-60 (Fed. Cir. 2012) (citing 35 U.S.C. § 282; *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2245 (2011)).[40] Clear and convincing evidence must place "an abiding conviction [in the fact finder] that the truth of [the] factual contentions are highly probable." *Proctor & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009) (citations omitted). The burden of establishing invalidity remains with the party asserting invalidity and exists at every stage of the litigation. *Kimberly-Clark Worldwide, Inc. v. First Quality Baby Prods., LLC*, 660 F.3d 1293, 1295 (Fed. Cir. 2011) (second alteration in original) (citations omitted).

B. The Written Description/Enablement Requirement

35 U.S.C. § 112 requires that a patent specification contain a written description of the claimed invention.[41] This requirement "serves to ensure that the inventor had possession, as of

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[40] 35 U.S.C. § 282(a) provides:

> A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.

[41] 35 U.S.C. § 112(a) provides:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

the filing date of the application relied on, of the specific subject matter later claimed by him; how the specification accomplishes this is not material." *In re Alton*, 76 F.3d 1168, 1172 (Fed. Cir. 1996) (quoting *In re Wertheim*, 541 F.2d 257, 262 (C.C.P.A. 1976)) (internal quotation marks omitted). In order to satisfy the written description requirement, "the [patent] applicant does not have to utilize any particular form of disclosure to describe the subject matter claimed, but the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *Id.* (quotations omitted).

The Federal Circuit has stated the standard for determining whether the written description requirement has been met as follows:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. . . . The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter."

In re Hayes Microcomputer Prods., Inc. Patent Litig., 982 F.2d 1527, 1533 (Fed. Cir. 1992) (quoting *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991)) (alterations in original). "Thus, an inventor is not required to describe every detail of his invention." *Id.* at 1534. Additionally, "examples are not necessary to support the adequacy of a written description." *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006).

35 U.S.C. § 112 also requires that a patent specification enable a person skilled in the art to make and use the claimed invention. "Invalidity for lack of enablement is a conclusion of law and must be supported by facts proved by clear and convincing evidence, for the grant of the patent by the PTO carries with it the presumption of validity including compliance with § 112." *N. Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990). "The enablement

requirement is satisfied when one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation." *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1244 (Fed. Cir. 2003) (quoting *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1998)).

The factors for determining whether undue experimentation is required include:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d at 737.

Further, the question of enablement does not turn on whether the accused product is enabled. Instead, "[t]o be enabling, the specification of the patent must teach those skilled in the art how to make and use the *full scope* of the claimed invention without undue experimentation." *Durel Corp. v. Osram Sylvania Inc.*, 256 F.3d 1298, 1306 (Fed. Cir. 2001) (quoting *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (alteration in original) (emphasis in original). Thus, it is the asserted claims rather than the accused device which must be enabled by the patent-in-suit.

C. Invalidity Analysis

As an initial matter, I find that Watson Florida improperly invokes the Watson ANDA Product when arguing invalidity. Applying the law recited above, it is not the Watson ANDA Product that must be enabled under § 112; rather, it is Claims 1 and 3 of the '720 Patent that must be enabled.

Notwithstanding, the Court finds that Watson Florida has not proven by clear and convincing evidence that the '720 Patent specification fails to convey to a person skilled in the art

that the named inventors invented the pharmaceutical compositions and processes covered by Claims 1 and 3. Additionally, Watson Florida has not proven by clear and convincing evidence that the '720 Patent specification fails to enable a person skilled in the art to make and use the pharmaceutical compositions and processes covered by Claims 1 and 3. Thus, Watson Florida has not proven by clear and convincing evidence that Claims 1 and 3 are invalid under 35 U.S.C. § 112.

Worth noting and relevant to the Court's analysis is the testimony of Defendants' expert Dr. Kibbe. Specifically, Dr. Kibbe unequivocally testified that "[t]he example of the '720 Patent and the specifications will allow you to make a product that would fit [Claim 1]." (Trial Tr. Day 5 at 113:12-13 (Kibbe Cross)). Dr. Kibbe also testified as such with regard to Claim 3. In fact, during cross examination, Plaintiffs' counsel walked Dr. Kibbe through each aspect of Claim 1 and compared it to Example 1 from the '720 Patent. Dr. Kibbe agreed that each part of Claim 1 was provided for and taught in Example 1. (Trial Tr. Day 5 at 109:9 to 111:16 (Kibbe Cross)).

V. CONCLUSION

Based upon the Court's findings set forth above, Plaintiffs have established by a preponderance of the evidence that the Defendants[42] have infringed Claims 1 and 3 of the '720 Patent. Additionally, Defendants have failed to prove by clear and convincing evidence that the Patent is invalid for lack of written description and/or enablement. For these reasons, Plaintiffs are entitled to the requested injunctive relief. However, the Court declines to make a finding of

[42] While it was only Watson Florida that filed the ANDA, the Court declines to distinguish the conduct of each Watson entity, as each Defendant induced or contributed to the construction of the Watson ANDA Product and the filing of the Watson ANDA.

willful infringement for purposes of awarding attorney's fees. Nor is this otherwise an "exceptional case" under 35 U.S.C. § 285.[43]

Final judgment shall issue by separate order.

DONE AND ORDERED in Chambers at West Palm Beach, Florida, this 9 day of May, 2013.

DONALD M. MIDDLEBROOKS
UNITED STATES DISTRICT JUDGE

Copies to: Counsel of Record

[43] 35 U.S.C. § 285 provides: "The court in exceptional cases may award reasonable attorney['s] fees to the prevailing party." Furthermore, 35 U.S.C. § 271(e)(4) specifically states that when infringement is based on the filing of an ANDA, "a court may award attorney fees under section 285." *Id.* The Federal Circuit has held that "the mere fact that a company has filed an ANDA application or certification cannot support a finding of willful infringement for purposes of awarding attorney's fees pursuant to 35 U.S.C. § 271(e)(4)." *Glaxo Grp. Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1350-51 (Fed. Cir. 2004). While Plaintiffs offered evidence that Defendants reverse-engineered Shire's Lialda® product, I do not find these actions remarkable in the context of attempting to develop a bioequivalent generic drug. There was also evidence of steps taken by Defendants to avoid infringement. I therefore decline to make a finding of willfulness.