IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

TAKEDA PHARMACEUTICAL COMPANY LTD., TAKEDA PHARMACEUTICALS NORTH AMERICA, INC., TAKEDA PHARMACEUTICALS LLC, TAKEDA PHARMACEUTICALS AMERICA, INC., and ETHYLPHARM, S.A.,	)	
Plaintiffs,	)	
v.	)	Civ. No. 07-331-SLR
TEVA PHARMACEUTICALS USA, INC. and TEVA PHARMACEUTICAL INDUSTRIES LTD.,	)	
Defendants.	)	

Steven J. Balick, Esquire, John G. Day, Esquire, and Lauren E. Maguire, Esquire of Ashby & Geddes, Wilmington, Delaware. Counsel for Plaintiffs. Of Counsel for Plaintiffs Takeda Pharmaceuticals LLC and Takeda Pharmaceuticals America, Inc.: Stuart E. Pollack, Esquire of DLA Piper LLP, New York, New York. Of Counsel for Plaintiff Takeda Pharmaceutical Company, Ltd.: Arlene L. Chow, Esquire, Dillon Kim, Esquire, and Eric J. Lobenfeld, Esquire of Hogan and Hartson LLP, New York, New York; Phillippe Y. Riesen, Esquire of Hogan and Hartson LLP, Tokyo Japan. Of Counsel for Plaintiff Takeda Pharmaceuticals North America, Inc.: Chad J. Peterman, Esquire of Patterson Belknap Webb & Tyler LLP, New York, New York; Stuart E. Pollack, Esquire of DLA Piper LLP, New York, New York. Of Counsel for Plaintiff Ethypharm, S.A.: Paul A. Ragusa, Esquire, Lisa Kole, Esquire, and Sandra Lee, Esquire of Baker Botts, LLP, New York, New York; Arlene L. Chow, Esquire, Dillon Kim, Esquire, and Eric J. Lobenfeld, Esquire of Hogan and Hartson LLP, New York, New York; Phillippe Y. Riesen, Esquire of Hogan and Hartson LLP, Tokyo Japan.

Karen L. Pascale, Esquire, John W. Shaw, Esquire, and Josy W. Ingersoll, Esquire of Young, Conaway, Stargatt & Taylor LLP, Wilmington, Delaware. Counsel for Defendants and Counterclaim Plaintiffs. Of Counsel: John L. North, Esquire, Jeffrey J. Toney, Esquire, Ann G. Fort, Esquire and Laura F. Fritts, Esquire of Sutherland Asbill & Brennan LLP, Atlanta, Georgia.

OPINION

Dated: November 9, 2009
Wilmington, Delaware

ROBINSON, District Judge

I. INTRODUCTION

Takeda Pharmaceutical Company, Ltd., Takeda Pharmaceuticals North America, Inc., Takeda Pharmaceuticals LLC and Takeda Pharmaceuticals America, Inc. (collectively, "Takeda") are the exclusive licensees of U.S. Patent No. 5,464,632 ("the '632 patent"), which claims a rapidly disintegrating oral tablet.[1] Takeda is the holder of an approved New Drug Application ("the NDA")[2] for lansoprazole delayed release orally disintegrating tablets, which it sells under the trade name PREVACID® Solutab™. The Orange Book of the Food and Drug Administration ("FDA") lists, inter alia, the '632 patent in connection with the NDA. Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries, Ltd. (collectively, "defendants") filed an Abbreviated New Drug Application ("the ANDA")[3] with the FDA, seeking approval to market 15 and 30 milligram generic versions of PREVACID® Solutab™ ("the ANDA products"). On April 12, 2007 defendants notified Takeda and Ethylpharm S.A. (collectively "plaintiffs") of the factual contentions supporting defendants' allegations that the patents covering PREVACID® Solutab™ are invalid, unenforceable, or will not be infringed by the commercial manufacture, use or sale of the ANDA products. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV). In response, plaintiffs instituted this patent infringement suit against defendants pursuant to 35 U.S.C. § 271(e)(2)(A).[4]

---

[1]Plaintiff Ethylpharm S.A. owns the '632 patent.

[2]No. 21-428.

[3]No. 78-730.

[4]"(2) It shall be an act of infringement to submit – (A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section

Plaintiffs asserted the '632 patent, as well as U.S. Patent Nos. 4,628,098 ("the '098 patent"), 5,045,321 ("the '321 patent"), and 6,328,994 ("the '994 patent") against defendants. Defendants responded in kind with defenses of invalidity, unenforceability and noninfringement. The court determined, and the Federal Circuit affirmed, that defendants infringed claim 10 of the valid and enforceable '098 patent. (D.I. 121 at ¶5) The court further concluded that plaintiffs failed to show that defendants infringed the '321 patent. (*Id.*) On February 27, 2009, the court entered a stipulated order, recognizing plaintiffs' dismissal of any allegations of infringement of the '994 patent, as well as the voluntary dismissal of defendants' invalidity and unenforceability defenses. (D.I. 94)

The '098 patent, which claims the active compound lansoprazole, expired on May 10, 2009. However, the FDA granted plaintiffs an additional six months of pediatric exclusivity, resulting in an effective expiration date of November 10, 2009. After this exclusivity expires, the '632 patent exists as the final obstacle to the approval of defendants' ANDA.

The sole remaining issue in this dispute is whether the ANDA products infringe claim 1 of the '632 patent. A bench trial was conducted from March 9-10, 2009, principally to resolve this issue, which has been fully briefed post-trial. The court has jurisdiction pursuant to 28 U.S.C. §§ 1331, 1338(a) and 1400(b). Having considered the documentary evidence and testimony, the court makes the following findings of fact and conclusions of law pursuant to Fed. R. Civ. P. 52(a).

505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent[.]"

II. FINDINGS OF FACT

A. The Parties

Takeda Pharmaceutical Company, Ltd. is a Japanese corporation with its principal place of business in Osaka, Japan. Takeda Pharmaceuticals North America, Inc. and Takeda Pharmaceuticals America, Inc. are Delaware corporations, each having a principal place of business in Deerfield, Illinois. Takeda Pharmaceuticals LLC is a limited liability company formed under the laws of the State of Delaware, with its principal place of business in Deerfield, Illinois. Takeda focuses primarily upon the research, development, marketing, purchase and sale of pharmaceutical products. (D.I. 97 at ¶¶ 1-4)

Ethylpharm S.A., the owner of the '632 patent, is a corporation formed under the laws of the nation of France, which has its principal place of business in Houdan, France. The business activities of Ethylpharm S.A. include the research, development, manufacturing, and licensing of pharmaceutical products. (*Id.* at ¶ 5)

Teva Pharmaceuticals Industries, Ltd. is an Israeli corporation with its principal place of business in Petach Tikva, Israel. Teva Pharmaceuticals USA, Inc. is a Delaware corporation with its principal place of business in North Wales, Pennsylvania. Teva Pharmaceuticals USA, Inc. is a wholly-owned subsidiary of Teva Pharmaceuticals Industries, Ltd. Teva engages primarily in the manufacturing and marketing of generic drugs. (*Id.* at ¶¶ 6-7)

B. The Technology at Issue

This dispute concerns a pharmaceutical formulation known as an orally

disintegrating tablet ("ODT"). ODT dosage forms allow for the oral delivery of an active pharmaceutical ingredient ("API"), in tablet form, to a patient without the typical accompanying requirement of water to assist with swallowing. (D.I. 141 at 78-79) Instead, an ODT disintegrates upon contact with saliva in the patient's mouth, creating an easy-to-swallow suspension. (*Id.* at 85) In doing so, ODT formulations avoid blocking the esophagus[5], a common pitfall associated with other tablet forms. The ODT functionality is particularly advantageous to individuals who traditionally experience difficulty in swallowing conventional tablets whole, serving as an alternative dosage form for, e.g., children, the elderly, or persons suffering from GERD.[6]

The prior art includes dosage forms comprised of freeze-dried and effervescent materials. (D.I. 141 at 85) Freeze-dried dosage forms suffered from several drawbacks; namely, moisture sensitivity, poor physical resistance and dosage limitations. (*Id.* at 86) The physical frailty of freeze-dried dosage forms, along with the lengthy process and specialized equipment required to manufacture such, resulted in considerable production costs. (*Id.*) Effervescing agents also endured moisture sensitivity issues and required strong, impermeable blister packs to preserve their integrity. (*Id.* at 87) Furthermore, the generally unpleasant taste and high sodium content left much to be desired with the effervescent formulations. (PTX 1 at col. 3:15-20)

---

[5]Aside from the obvious danger of choking, tablets which become lodged in the esophagus may result in a delay in absorption of the active ingredient and ulceration. (PTX 1 at col. 2:64 - col. 3:6)

[6]Gastro Esophogeal Reflux Disease.

C. The '632 Patent

On November 7, 1995, the United States Patent and Trademark Office ("the PTO") issued the '632 patent, entitled "Rapidly Disintegratable Multiparticular Tablet," to Laboratoires Prographarm[7], the assignee of the named inventors Gerard Cousin, Etienne Bruna, and Eduoard Gendrot. Subsequently, the patentee requested reexamination of the '632 patent. The PTO, determining that a substantial new question of patentability existed, granted the request, and the claims of the '632 patent were amended in light of 72 previously unconsidered prior art references. Claim 1, the sole independent claim of the reexamined '632 patent, reads as follows:

> A rapidly disintegratable tablet for oral administration and disintegration in the buccal cavity without the use of water, wherein said tablet comprises an active substance and a mixture of non-effervescent excipients and permits to obtain reduced ph influence in the digestive tract and reduced influence of viscosity, said active substance being multiparticulate and in the form of coated microcrystals, or coated microgranules and **wherein said mixture of excipients comprises a disintegrating agent and swelling agent** which are responsible for the disintegration of the tablet with the saliva present in the mouth, to achieve in less than 60 seconds a suspension easy to swallow.

(emphasis added)

The '632 patent describes an ODT formulation in which coated microgranules are compressed together with other excipients to form a tablet. This dosage form ameliorates many of the issues present in the prior art. The microgranules are created by application of an enteric coating to the API. (*Id.* at 83-84) This polymeric film can mask any undesirable taste characteristics of the API. (*Id.*) The coating further serves to protect moisture and acid sensitive drugs, allowing the API to dissolve in the intestine

---

[7]Ethylpharm S.A. subsequently acquired Laboratoires Prographarm.

by preventing early dissolution in the mouth and stomach. (*Id.*) Likewise, the process[8] used to manufacture the ODT dosage form allows for a much greater production rate than that of the freeze-dried dosage form. (*Id.* at 89-90)

The ODT's rapid rate of disintegration is attributable to the presence of both a disintegrating agent and a swelling agent. (*Id.* at 91) The disintegrating agent induces the disintegration upon penetration of the tablet by saliva, while the swelling agent[9] amplifies the process such that it completes within 60 seconds. (*Id.* at 92) Once the excipients fully disintegrate, the patient then swallows the remaining suspension of microgranules.

PREVACID® SoluTab™, proprietary to plaintiffs, is an ODT dosage form. Lansoprazole, the API in PREVACID® SoluTab™, is a proton pump inhibitor[10] that holds indications for various gastroenterological diseases. (*Id.* at 61) Defendants' ANDA products contain multiparticulate lansoprazole, protected by an enteric coating, in 15 and 30 milligram doses. The ANDA products also contain several excipients;

---

[8]The microgranules and excipients are fed into a tabletting machine, which quickly compresses the powder mixture and ejects it in tablet form. (*Id.* at 89-90)

[9]The swelling agent also serves a secondary role in which it provides cushioning during the compression process used to create the tablets. Without this cushioning, the microgranules could rupture or crack, exposing the vulnerable API, under the 2,000 - 3,000 pounds of force required to make a single tablet. (*Id.* at 91)

[10]Proton pump inhibitors prevent gastric parietal cells from pumping acid into the gastrointestinal tract, and relieve symptoms of several common debilitating diseases such as duodenal ulcers, gastric ulcers, GERD, Zollinger-Ellison syndrome and erosive esophagitis.

however, the parties have agreed that StarLac®[11], which accounts for a substantial percentage by weight of each tablet, is the excipient responsible for the rapid disintegration of the ANDA products. (D.I. 132 at 6; D.I. 135 at 5)

StarLac® is created by coprocessing[12] lactose monohydrate and maize starch. (D.I. 141 at 98) While lactose and starch are well-known to formulators, coprocessing these classic pharmaceutical ingredients results in an excipient whose rate of disintegration is unmatched by a simple physical blend.[13] (*Id.* at 110) Coprocessing allows excipients to interact at a subparticle level, while still retaining separate chemical identities. (*Id.* at 110-112) This subparticle interaction causes a physical transformation which can eliminate or minimize undesirable properties (such as brittleness) and amplify desirable characteristics (such as rate of disintegration). (*Id.* at 111)

Images taken by a scanning electron microscope reveal that coprocessing lactose monohydrate and maize starch results in three distinct constituents bound together in a porous matrix: amorphous lactose, crystalline lactose and starch. (PTX

---

[11]StarLac® is the joint creation of Meggle GmbH and Roquette Frères, two European producers specializing in the development and manufacturing of pharmaceutical ingredients and excipients.

[12]Coprocessing here involves the addition of alpha-lactose monohydrate and maize starch (85 and 15 percent by weight, respectively) to a cold water bath. The starch, insoluble at these conditions, disperses into the bath, while the lactose fully dissolves. The finished product is obtained by spray-drying this suspension. (D.I. 141 at 113-114)

[13]StarLac® causes the disintegration of the ANDA products within 60 seconds. (*Id.* at 127). Both parties agree that a physical blend of lactose and maize starch would display a lesser rate of disintegration.

122 at 2) Defendants' expert, Dr. Walter Chambliss, testified on cross as to the configuration of these materials in StarLac®, noting that the crystalline lactose and starch are embedded in the amorphous lactose. (D.I. 142 at 303 (explaining that "amorphous lactose is the glue holding [StarLac®] together"))

III. CONCLUSIONS OF LAW

A. Infringement

"'It shall be an act of infringement to submit' an ANDA to the FDA seeking approval 'to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.'" *Cephalon, Inc. v. Watson Pharmaceuticals, Inc.*, 2009 WL 1838352 *7 (D. Del. Apr. 3, 2009) (quoting 35 U.S.C. § 271(e)(2)). To determine whether a composition identified in an ANDA is a composition claimed in a patent, the court conducts the familiar two-step infringement inquiry: first, the court construes the patent claims; second, it compares the construed claims to the accused product to determine whether every claim limitation is found in the accused product. *See, e.g., Roche Palo Alto LLC v. Apotex, Inc.*, 531 F.3d 1372, 1377 (Fed. Cir. 2008) (condoning use of the two-step infringement inquiry in the ANDA context). The patent owner has the burden of proving infringement and must meet its burden by a preponderance of the evidence. *SmithKline Diagnostics, Inc. v. Helena Lab. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988) (citations omitted).

With respect to the first step of the infringement inquiry, defendants have stipulated that the ANDA products contain many of the limitations of claim 1, directing

arguments only to the phrase ". . . wherein said mixture of excipients comprises a disintegrating agent and swelling agent . . . ." (D.I. 107) Although the parties have parsed this language, the court will construe this limitation in its entirety.

1. Claim Construction

The court construes the words of a claim according to "their ordinary and customary meaning." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005). A claim term's "ordinary and customary meaning" "is the meaning that the term would have to a person of ordinary skill in the art in the question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id.* "[T]he person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Id.* Where "the meaning of a claim term as understood by persons of skill in the art is . . . not immediately apparent," the court turns to publicly-available sources to ascertain the meaning, including "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* at 1314 (quotation marks omitted).

Upon application of these principles, the court concludes that the limitation **"wherein said mixture of excipients comprises a disintegrating agent and swelling agent"** means a combination or blend of non-effervescent inert substances or vehicles which includes at least one substance that causes disintegration and at least one substance that, when contacted with liquid, absorbs the liquid and expands in

volume.

The above construction is consistent with the language of the claim, the specification and the prosecution history. Claim 1 provides that the "mixture of excipients comprises a disintegrating agent and swelling agent which **are** responsible for the disintegration of the tablet . . . ." The use of the plural "are" refers to multiple agents, as opposed to the singular mixture of excipients, signifying that there must be at least one disintegrating agent and at least one swelling agent which are responsible for the disintegration of the ODT.[14] The specification likewise refers to both a disintegrating agent and a swelling agent: "The disintegration rate is obtained due to a mixture of excipients or vehicles which comprises generally **a** disintegrating agent . . . and **a** swelling agent . . . ." (PTX 1 at col. 1:13-16) (emphasis added); "the mixture of excipients comprises **one** or several disintegrating agents . . ., **one** or several swelling agents . . ., and possibly a direct compression sugar . . . ." (*Id.* at col 1:47-55) (emphasis added).

Finally, the prosecution history of the '632 patent is consistent with the requirement that there be both a disintegrating agent and a swelling agent. The original application required neither a disintegrating agent nor a swelling agent in claim 1; this limitation was initially contained only in the dependent claims of the application, which required either a disintegrating agent or a swelling agent. (D.I. 115, ex. 2 at

---

[14]The use of the word "comprises" means that, while the mixture of excipients must include at least one disintegrating agent and at least one swelling agent, it may permissibly include other types of excipients, as well as more than one disintegrating agent and more than one swelling agent. *See Cias, Inc. v. Alliance Gaming Corp.*, 504 F.3d 1356, 1360-61 (Fed. Cir. 2007).

TVLODT072683) An examiner's rejection prompted an amendment to claim 1, which read upon allowance:

> A rapidly disintegratable tablet . . . wherein said tablet comprises an active substance and a mixture of non-effervescent excipients . . . and wherein said mixture of excipients . . . are selected from the group consisting [of] **at least one** disintegrating agent and **at least one** swelling agent.

(PTX 1 at col. 7:51-62) (emphasis added) During reexamination, the patentee cancelled the Markush group and further limited claim 1 to require both **a** disintegrating agent and **a** swelling agent. (PTX 1, Reexamination Certificate at col. 1:23 - col 2:17)

With respect to the proper construction of the disintegrating agent and the swelling agent, it is noteworthy that the most explicit evidence within the four corners of the specification as to the characteristics of these agents consists of a single passage which provides that, in a preferred embodiment, "the mixture of excipients comprises one or several disintegrating agents of the carboxymethylcellulose type or insoluble reticulated PVP type, one or several swelling agents which may consist of a carboxymethylcellulose, a starch, a modified starch, for instance a carboxymethylated starch, or a microcrystalline cellulose . . . ." (PTX 1 at col 1:47-50) The examples given of swelling agents are consistent with the ordinary meaning of such, that is, a substance which, when contacted with liquid, absorbs the liquid and expands in volume. The parties do not dispute this construction.

The parties do take issue as to whether a disintegrating agent, as contemplated by claim 1, must "cause" disintegration or merely "facilitate" disintegration. The extrinsic references identified by the parties define "disintegrating agent" as a substance that both "facilitates" and "causes" the breakup or disintegration of a tablet. (D.I. 115, ex. 5

at 1606; PTX 61 at 218) Looking to the specification, the examples identified as disintegrating agents are known in the art as "super-disintegrants," i.e., excipients whose disintegrating characteristics bear a strong causal relationship to the breakup of a tablet. (D.I. 115, ex. 16 at 109-10) Super-disintegrants are classified as such due to the comparatively low amount of excipient required to achieve the disintegration of a formulation.[15] (PTX 56)

Like the specification, the prosecution history[16] is more consistent with a construction requiring an agent that "causes" disintegration. During prosecution, the examiner rejected the claims of the application leading to the '632 patent ("the application") as unpatentable over U.S. Patent No. 5,073,374 granted to McCarty ("McCarty"). (D.I. 115 at TVLODT072765) McCarty teaches a quickly dissolving tablet comprising a soluble API, a lubricant and "a soluble, directly compressible tablet excipient." (PTX 85 at col. 2:8-12) The soluble excipient disclosed in McCarty "is typically a sugar, such as sucrose or lactose." (*Id.* at col 2:14-15) Although claim 1 of McCarty describes a buccal tablet where ". . . **disintegration** occurs from 0.5 to 5

---

[15]Super disintegrants can cause effective disintegration at concentrations of 2-4 wt%. (PTX 56)

[16]The Federal Circuit endorses use of the prosecution history to assist the person of ordinary skill in the art to assess the scope of an issued patent. *See Hockerson-Halberstadt, Inc. v. Avia Group Int'l*, 222 F.3d 951, 957 (Fed. Cir. 2000) (noting that "[t]he prosecution history constitutes a public record of the patentee's representations concerning the scope and meaning of the claims, and competitors are entitled to rely on those representations when ascertaining the degree of lawful conduct, such as designing around the claimed invention."). The Federal Circuit has further explained that this "use of the prosecution history ensures that claims are not construed one way in order to obtain their allowance and in a different way against accused infringers." *See Chimie v. PPG Indus.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005).

minutes after administration" (emphasis added), in traversing the rejection, the patentee nevertheless alleged that McCarty "clear[ly] . . . does not teach disintegrating agents." (D.I. 115 at TVLODT072765)

In light of the descriptions of "disintegrating agent" given in the specification and the prosecution history, the court concludes that a causal relationship must exist between the disintegrating agent and the act of disintegration. Put another way, excipients that facilitate disintegration, but are not known in the art to cause disintegration as "disintegrating agents," will not fall within this limitation.

2. Existence of Infringement

The mechanism through which StarLac® breaks apart is hotly disputed. While StarLac® must contain both a swelling agent and a disintegrating agent in order to infringe the '632 patent, the parties direct most of their arguments towards the identification of the disintegrating agent.[17] According to Dr. Chambliss, the driving force behind the disintegration of StarLac is the presence of starch. (D.I. 142 at 233) Once the ANDA products are placed on the tongue, the starch begins to draw moisture into the tablet through a wicking action. (*Id.*) This moisture then "breaks the bonds that have been formed during compression, and the tablet falls apart." (*Id.*) Dr. Chamblis generally views the disintegration of the tablet as occuring through "a rapid swelling and disruption of the StarLac® particles." (*Id.* at 247) Irrespective of this swelling, Dr. Chambliss contends that starch's method of action is more akin to disintegrating than swelling. (*Id.* at 232) Lactose, on the other hand, does not appreciably contribute to

[17]Defendants do not seriously contest that starch could meet the swelling agent limitation. (D.I. 142 at 231-32)

the disintegration, but rather acts as a filler that provides "an acceptable crushing force" (i.e. sufficiently holds the tablet together). (*Id.* at 239-40)

In support of this mechanism, Dr. Chambliss relies upon documents issued by manufacturer Roquette, as well as third party investigations of StarLac®. An informational release authored by a Roquette senior manager describes StarLac® as providing "for the use of well-known native corn starch in the place of an expensive super-disintegrant." (DTX 99) An independent study regarding directly compressible excipients explains that StarLac® has several advantages, including "an acceptable crushing force due to its lactose content [and] its rapid disintegration depending on starch." (DTX 49 at 88)[18] According to Dr. Chambliss, this study attributes these advantages to the "ideal proportions" in StarLac® (85% lactose and 15% starch). (D.I. 142 at 241-42; DTX 49) Garnering support for his theory generally, Dr. Chambliss points to references which identify starch as a traditional disintegrating agent. (DTX 95; DTX 99) Several references exclude lactose altogether from listings of tablet disintegrants, classifying lactose as either a binder, diluent or filler. (DTX 57; DTX 95; DTX 99; DTX 52; DTX 59)

Dr. Reza Fassihi, by contrast, testified for plaintiffs that the lactose in StarLac® functions as a disintegrant, while starch acts as a swelling agent. (D.I. 141 at 108) According to Dr. Fassihi, lactose is well known in the art to have disintegrating properties. (*Id.* at 117) Dr. Fassihi identifies several references with which he purports to support this premise. A table in *Modern Pharmaceutics*, a treatise recognized in the

---

[18]This study relied upon data obtained from a independent investigation published in 2004 in the AAPS Pharmaceutical Sciences Journal. (DTX 53)

field, compares various properties of certain diluents, among which are several forms of lactose. (PTX 65 at 364) The table assigns a numeric value[19] indicating the strength of the diluent with respect to the property in question. (*Id.*) The different forms of lactose were identified as having disintegration values of 3-4.[20] (*Id.*) Other references passingly refer to lactose as a disintegrating agent. (PTX 188 at 440 ("lactose, Primojel and Avicel pH101 were added as disintegrating agents")); (PTX 177 at 124 ("[o]nly lactose and Avicel pH 101 were added as disintegrating agents"))

Dr. Fassihi further opines that this disintegrating functionality is enhanced by coprocessing lactose with starch.[21] As previously discussed, StarLac® contains amorphous lactose, crystalline lactose and starch. (PTX 122 at 2) Due to the highly energetic nature of amorphous materials, Dr. Fassihi explains, amorphous lactose will rupture when exposed to water and disintegrate very quickly. (D.I. 141 at 127) Because amorphous lactose is the "glue holding [StarLac®] together," and because StarLac® comprises more than 50% of the ANDA products, logically, once this "glue" is gone, the entire tablet will disintegrate. (*Id.* at 140-42) Thus, Dr. Fassihi theorizes that amorphous lactose provides the disintegrating function in StarLac®. (*Id.* at 140-43) Dr. Fassihi identifies starch as the swelling agent, noting that even Dr. Chambliss readily

---

[19]The diluents are graded on a scale from 5, the highest, to 0, indicating a complete lack of the property.

[20]Tellingly, though, a chapter in this same treatise, which discusses at length disintegrating agents, identifies starch as such but makes no reference to lactose. (*Id.* at 372-79)

[21]Dr. Fassihi seemingly performed no experiments upon StarLac® to verify this theory.

admits that starch will "swell[] between 5-10%" when contacted with a liquid. (D.I. 142 at 232)

The evidence demonstrates that, although StarLac® causes the disintegration of the ANDA products within 60 seconds, it is questionable exactly which component induces this disintegration. While plaintiffs have shown that lactose has some disintegrative properties, the record as a whole indicates that the prior art did not characterize lactose as a disintegrating agent. It is insufficient that an excipient merely possess a tendency to disintegrate; the excipient must actually cause the disintegration of the formulation in order to read upon this limitation of the '632 patent. The court is likewise skeptical of Dr. Fassihi's untested theory attributing the disintegration of the ANDA products to the amorphous lactose content in StarLac®. Indeed, it is at least as likely that starch, traditionally known in the art as a disintegrating agent, fills this role.

Even if plaintiffs could convincingly show that lactose caused the disintegration of StarLac®, the patentee's disavowal of lactose in order to distinguish McCarty during prosecution clearly shows that lactose cannot be a disintegrating agent within the meaning of the '632 patent.[22] Finally, because the starch in StarLac® cannot meet both

---

[22]Plaintiffs argue that it is reconcilable, in light of the McCarty traversal, to conclude that the lactose in StarLac® reads upon the disintegrating agent limitation. Plaintiffs explain that the dissolving tablet taught by McCarty is properly distinguishable from the disintegrating formulation of the '632 patent. Because the tablet in McCarty completely dissolves, plaintiffs contend that lactose acts not as a disintegrating agent, but as a dissolving component. (D.I. 132 at 20) By contrast, the formulation claimed by the '632 patent disintegrates upon introduction to saliva, leaving behind the insoluble microgranules. Thus, according to plaintiffs, lactose has a different role in each of the two formulations.

The court disagrees. Certainly, there is a distinction between formulations, as a whole, that dissolve and those that disintegrate. However, in this instance, the patentee chose to distinguish its invention from McCarty by arguing that the reference failed to

the disintegrating agent and the swelling agent limitations of the '632 patent, a finding of noninfringement is proper in this case.

IV. CONCLUSION

For the aforementioned reasons, plaintiffs have failed to prove, by a preponderance of the evidence, that defendants' ANDA products infringe the '632 patent. An appropriate order shall issue.

---

teach "disintegrating agents." (D.I. 115 at TVLODT072765) The method of action for lactose is consistent in both formulations, i.e., it is a soluble component that dissolves upon exposure to moisture. (D.I. 141 at 143) Therefore, if lactose is not a disintegrating agent with respect to the McCarty reference, it would be improper to characterize it as such in the ANDA products.