UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

ELI LILLY AND COMPANY,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Case No. 1:16-cv-03460-TWP-MPB
	)	
HOSPIRA, INC.,	)	
	)	
Defendant.	)	

ENTRY ON CROSS MOTIONS FOR SUMMARY JUDGMENT

Before the Court are the parties' cross-motions for summary judgment. Eli Lilly and Company ("Lilly") initiated this Hatch-Waxman litigation against Defendant Hospira, Inc. ("Hospira") for infringement of Lilly's U.S. Patent 7,772,209 ("the '209 Patent"). On April 6, 2018, Hospira filed a Motion for Summary Judgment of Non-Infringement on its New Drug Application ("NDA") No. 208746, on the bases that there is no plausible theory pled under which Hospira would infringe the patent in suit and the doctrine of equivalents does not expand the scope of Lilly's patent to include Hospira's product. (Filing No. 73.) On April 27, 2018, Lilly filed a Cross-Motion for Summary Judgment of Infringement. (Filing No. 78.) For the reasons stated below, the Court **grants** Lilly's Cross-Motion for Summary Judgment, and **denies** Hospira's Motion for Summary Judgment.

I. BACKGROUND

The '209 Patent describes a method of administering the chemotherapy drug, pemetrexed disodium, with a pretreatment regimen of vitamin B_{12} and folic acid (the "pretreatment regimen"), which is marketed by Lilly under the trade name ALIMTA®. The '209 Patent has been the subject of previous trials before this Court. *See Eli Lilly and Co. v. Teva Parenteral Medicines, Inc.*, 126

F. Supp.3d 1037, 1038 (S.D. Ind. 2015).[1] Two of those cases specifically concerned generic drug manufacturers that sought to market a generic version of ALIMTA® including labeling that induced physicians to direct patients to take folic acid and vitamin B_{12} in accordance with the pretreatment claims in the '209 Patent. Specifically, in the *Teva* case, the pretreatment regimen and whether the steps of the claimed method could be attributed to a single actor was at issue. *Id.* On February 1 and 2, 2018, this Court held a bench trial in *Eli Lilly & Co. v. Dr. Reddy's Laboratories, Ltd.*, No. 1:16-cv-308-TWP-MPB (the "Dr. Reddy's Case") involving primarily the same alleged infringing drug product at issue in this action: pemetrexed ditromethamine.[2]

During prosecution of its patent application for ALIMTA®, the U.S. Patent and Trademark Office originally rejected claim 2 of the '209 Patent as being anticipated by a prior art article, Arsenyan *et.al.* ("Arsenyan"). Arsenyan concerned the administration of the compound methotrexate.[3] (Filing No. 76-3 at 105.) To avoid rejection of its patent in view of Arsenyan, Lilly narrowed the scope of its claims from a broad category of antifolates to specifically pemetrexed disodium. (Filing No. 76-3 at 123.)

Similar to the issue in Dr. Reddy's Case, Hospira has also developed and designed a competing pemetrexed drug product, which uses a salt base, tromethamine, rather than the sodium base contained in Lilly's product.[4] Hospira seeks to market its product in the form of a new product that uses pemetrexed ditromethamine, unlike the generic drugs in previous trials before the Court.

[1] The '209 Patent is also the subject of other pending infringement suits pending before this Court.

[2] Because Hospira has conceded that many of the case-dispositive questions were all resolved against its interest in the Court's summary judgment ruling in the Dr. Reddy's Case, the Court relies heavily on the analysis contained therein in resolving the present cross-summary judgment motion in this case. (*See* Filing No. 79-3.)

[3] Both methotrexate and pemetrexed fall within the broader antifolate group, but they target different enzymes. (*See* Filing No. 79 at 24.)

[4] Although Hospira's drug label is slightly different, Hospira's drug product is identical to that in the Dr. Reddy's Case. (Filing No. 74-1 at 15.)

In large part, the issues in the present case and the Dr. Reddy's Case are the same. However, unlike Dr. Reddy's label, Hospira's label instructs that it can be reconstituted in saline solution (like ALIMTA®) in addition to 5% dextrose solution (like Dr. Reddy's product). (Filing No. 49-29; Filing No. 74-1 at 15-16.)

A point of contention between the parties is whether pemetrexed ditromethamine was excluded (thus, designated public use) from the claims during patent prosecution by Lilly's specification and narrowing amendment from the term "antifolates" to "pemetrexed disodium". The liquid solution of both chemical compounds results in pemetrexed treatment, but the powdered solid form of the two products differ as a result of the different salt compounds used. The patient receives the liquid solution intravenously. Both products are sold in solid form. (Filing No. 74-1 at 17; Filing No. 79 at 14.) Claim 12 of the '209 Patent, a dispositive issue (agreed by the parties) regarding whether or not Hospira's product infringes was construed in the Dr. Reddy's Case by this Court. (Filing No. 79-3 at 6.) Claim 12 reads as follows:

> 12. An improved method for administering pemetrexed disodium to a patient in need of chemotherapeutic treatment, wherein the improvement comprises:
>
> a) administration of between about 350 µg and about 1000 µg of folic acid prior to the first administration of pemetrexed disodium;
>
> b) administration of about 500 µg to about 1500 µg of vitamin B_{12}, prior to the first administration of pemetrexed disodium; and
>
> c) administration of pemetrexed disodium.

(Filing No. 1-1 at 9). The Court construed administration of pemetrexed disodium to refer to a liquid administration of pemetrexed disodium. (No. 1:16-308-TWP-MPB, ECF 199 at 9.) In the claim construction, the Court did not address the science of what happens when pemetrexed disodium is dissolved in aqueous solution in construing claim 12. *Id.* at 8-9. Nevertheless, Hospira and Lilly agree that based on the Court's construction in the Dr. Reddy's Case, that claim 12 would

necessarily encompass any solution containing pemetrexed and sodium ions because it is undisputed that when pemetrexed disodium is dissolved in solution, pemetrexed disodium would not exist as an ionically bonded compound. (Filing No. 79 at 9; Filing No. 79-3 at 8). Rather the liquid solution contains pemetrexed and disodium (or tromethamine) ions disassociated from one another.[5] *Id.* Thus, the solution that is administered to the patient would not contain pemetrexed disodium as an ionically bonded salt, and instead would contain disassociated pemetrexed and sodium ions in solution. The Court directs the parties to the Dr. Reddy's Case for the analysis of the claim construction ruling, which binds the identical claim at issue in this case.

II. LEGAL STANDARD

The purpose of summary judgment is to "pierce the pleadings and to assess the proof in order to see whether there is a genuine need for trial." *Matsushita Electric Industrial Co. v. Zenith Radio Corp.*, 475 U.S. 574, 587 (1986). Federal Rule of Civil Procedure 56 provides that summary judgment is appropriate if "the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." *Hemsworth v. Quotesmith.Com, Inc.*, 476 F.3d 487, 489-90 (7th Cir. 2007). In ruling on a motion for summary judgment, the court reviews "the record in the light most favorable to the nonmoving party and draw[s] all reasonable inferences in that party's favor." *Zerante v. DeLuca*, 555 F.3d 582, 584 (7th Cir. 2009) (citation omitted). However, "[a] party who bears the burden of proof on a particular issue may not rest on its pleadings, but must affirmatively demonstrate, by specific factual allegations, that there is a genuine issue of material fact that requires trial." *Hemsworth*, 476 F.3d at 490 (citation omitted). "In much the same way that a court is not required to scour the

[5] Hospira does not agree with this Court's claim construction ruling, however it concedes that under this construction its product would infringe. (Filing No. 79-3 at 7-8.)

record in search of evidence to defeat a motion for summary judgment, nor is it permitted to conduct a paper trial on the merits of a claim." *Ritchie v. Glidden Co.*, 242 F.3d 713, 723 (7th Cir. 2001) (citation and internal quotations omitted). Finally, "neither the mere existence of some alleged factual dispute between the parties nor the existence of some metaphysical doubt as to the material facts is sufficient to defeat a motion for summary judgment." *Chiaramonte v. Fashion Bed Grp., Inc.*, 129 F.3d 391, 395 (7th Cir. 1997) (citations and internal quotations omitted). This notion applies equally where, as here, opposing parties each move for summary judgment in their favor pursuant to Rule 56. *I.A.E., Inc. v. Shaver*, 74 F.3d 768, 774 (7th Cir. 1996).

III. DISCUSSION

Lilly argues that Hospira's product infringes under two theories: literal infringement and the doctrine of equivalents. (Filing No. 79 at 18, 23.) Hospira raises three non-infringement defenses to Lilly's infringement theories. (Filing No. 74-1 at 5.) The Court will address each argument in turn.

A. Literal Infringement

"Literal infringement requires a patentee to prove by a preponderance of the evidence that every limitation of the asserted claim is literally met by the allegedly infringing device." *Biovail Corp. Intern. v. Andrx Pharmaceuticals, Inc.*, 239 F. 3d 1297, 1302 (Fed. Cir. 2001). Lilly contends that Hospira's product will literally infringe when it is reconstituted in saline according to Hospira's proposed labeling instructions. (Filing No. 79 at 18.) It is undisputed as manufactured pemetrexed ditromethamine is a separate, distinct compound from the claimed pemetrexed disodium. (Filing No. 74-1 at 24; Filing No. 79 at 18.) Thus, in solid form Hospira's product does not contain pemetrexed disodium. Hospira's product may be reconstituted and diluted pursuant to

either saline preparation or dextrose preparation. (Filing No. 74-1 at 24.) Lilly contends that the saline preparation will literally infringe the '209 Patent.

Lilly has presented unrebutted expert testimony as to the chemical makeup of Hospira's product reconstituted in saline solution that would be administered to a patient. (Filing No. 78-1; Filing No. 78-2.) Additionally, Hospira concedes that under the Court's claim construction in the Dr. Reddy's Case, that its product, in accordance with its proposed labeling, literally infringes the '209 Patent. (Filing No. 79-3 at 12.) Saline solution contains sodium chloride, which also dissociates (at the molecular level) completely into sodium and chloride ions when dissolved in the solution. (Filing no. 79-2 at 12-13.) Because it is undisputed that, in liquid administration, pemetrexed is the active moiety that exerts chemotherapeutic effect to the patient, in that the pemetrexed dissociates from the ionic salt bond it was attached to, it makes no difference whether the ionic bond started as pemetrexed disodium or pemetrexed ditromethamine. (Filing No. 79-2 at 13.) With regards to the saline dilution and reconstitution, the resulting solutions in both instances would contain dissociated pemetrexed ions and sodium ions—that is pemetrexed disodium. *Id.* at 15. It is of no moment if the solution also contains tromethamine ions (as in Hospira's product), so long as the solution contains pemetrexed and a corresponding number of sodium ions (two per pemetrexed ion). *Id.* Accordingly, administering Hospira's NDA products reconstituted and diluted in saline literally infringe the '209 Patent. Thus, Lilly's Cross-Motion for Summary Judgment of literal infringement is **granted**.

B. Doctrine of Equivalents

"The doctrine of equivalents extends the right to exclude beyond the literal scope of the claims." *Johnson & Johnston Associates, Inc. v. R.E. Service Co., Inc.*, 285 F.3d 1046, 1053 (Fed. Cir. 2002). "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.*, 535 U.S. 722, 733 (2002). The doctrine of equivalents is restricted by the "all limitations" rule and the prosecution history estoppel rule by limiting the range of equivalents when claims have been narrowed. *See Pozen Inc. v. Par Pharmaceutical, Inc.*, 696 F.3d 1151, 1167. Hospira argues that Lilly's doctrine of equivalents infringement claim is foreclosed by prosecution history estoppel and the disclosure dedication rule. The Court will address each of these threshold arguments in turn.

1. Prosecution History Estoppel

Hospira presents defenses similar to those of Dr. Reddy's in the Dr. Reddy's Case. It is undisputed that Lilly narrowed its broader antifolates claim to pemetrexed disodium during prosecution to avoid Arsenyan prior art. It is also undisputed that Hospira's product would fall within the scope of the original antifolates claim. Under *Festo*, Lilly's narrowing amendment triggers a presumption of surrender that Lilly must rebut to sustain its doctrine of equivalents claim. *Festo*, 535 U.S. at 725. *Festo* held three exceptions to defeat prosecution history estoppel:

> The equivalent may have been unforeseeable at the time of the application; the rationale underlying the amendment may bear no more than a tangential relation to the equivalent in question; or there may be some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question. In those cases the patentee can overcome the presumption that prosecution history estoppel bars finding an equivalence.

Id. at 740-41. In contrast to Dr. Reddy's argument on prosecution history estoppel, Hospira agrees that there are three independent ways to overcome the presumption that prosecution history estoppel bars Lilly's doctrine of equivalents claim. (Filing No. 74-1 at 28.) Nevertheless, Hospira argues that Lilly cannot meet any of the three possible grounds for rebuttal to apply. *Id.* at 31. In the Dr. Reddy's Case, the Court found that the tangential exception applied, and the Court will focus on that exception in the case at bar.

Hospira contends that Lilly's amendment, made during prosecution of the '209 Patent, related *directly* to the alleged equivalent pemetrexed ditromethamine, rather than a tangential relationship because Lilly emphasized repeatedly that its invention concerned pemetrexed disodium. *Id.* at 33. Lilly responds that the rationale for amending the '209 Patent claims from "antifolate" to "pemetrexed disodium" bore no more than a tangential relation to the particular salt form of pemetrexed (disodium as claimed versus ditromethamine used by equivalent). (Filing No. 79 at 23.) Moreover, Lilly explains that a person of skill in the art ("POSA") would understand that the rationale for the amendment was to distinguish pemetrexed from other active antifolates such as methotrexate as it is undisputed that Arsenyan nor the prosecution history discuss different salt forms of pemetrexed. *Id*. at 24.

On this issue, in the Dr. Reddy's Case, the Court relied on *Regents of University of Cal. v. Dakocytomation Cal. Inc.*, where the federal circuit held that a patentee's narrowing amendment that centered on a method of blocking to avoid prior art that did not involve blocking was tangential to the particular nucleic acid used to accomplish the blocking. 517 F. 3d 1364, 1378 (Fed. Cir. 2008). The patent at issue in that case claimed "blocking nucleic acid" which was construed by the district court to involve human DNA, whereas the accused product used synthetic (not human) nucleic acids referred to as peptide nucleic acids. *Id.* The use of synthetic nucleic acids to accomplish the blocking method fell within the original broader claims, but was subsequently removed by the amendment. In reversing the district court's summary judgment of non-infringement, the federal circuit held "[t]he prosecution history therefore reveals that in narrowing the claim to overcome the prior art rejections, the focus of the patentees' arguments centered on the method of blocking—not on the particular type of nucleic acid that could be used for blocking." *Id.* Thus, the federal circuit found the narrowing amendment was tangential.

Lilly also cites another line of cases that demonstrate that "the tangentiality exception has routinely been applied in cases where the issued claims have been narrowed in a manner that excludes the accused equivalent." (Filing No. 79 at 26.) *See Insituform Technologies, Inc., v. CAT Contracting, Inc.*, 385 F.3d 1360 (Fed. Cir. 2004); *Pfizer Inc., v. Teva Pharmaceuticals U.S.A.*, Inc., 882 F. Supp. 2d 643 (D. Del. 2012). Lilly's amendment focused on distinguishing pemetrexed (the active antifolate) as opposed to methotrexate (a different antifolate) in that the '209 patent was drafted to protect a method of reducing toxicity associated with the administration of pemetrexed disodium. (Filing No. 79 at 28-29). A POSA would regard the salt form of the antifolate (pemetrexed) as peripheral to the amendment. *Id.* at 29. Because the tangentiality exception applies, an independent and dispositive basis under *Festo*, Lilly is not estopped from pursuing infringement under the doctrine of equivalents. The Court need not discuss Hospira's remaining arguments regarding the other two *Festo* exceptions (the foreseeability of tromethamine or that Lilly could have drafted the '209 Patent to claim pemetrexed ditromethamine).

2. Disclosure Dedication Doctrine

Similar to the Dr. Reddy's Case, Hospira also argues a second threshold issue in that Lilly is barred from pursuing infringement under the doctrine of equivalents because of the disclosure-dedication rule. However, Hospira has invoked the doctrine on a different aspect of the '209 Patent's specification than the one relied on by Dr. Reddy's. Specifically, Hospira contends that the "'209 patent specification unambiguously discloses the administration of any 'antifolate'"[6] and further, that Lilly's claim to pemetrexed disodium dedicated to the public use of any antifolate other than pemetrexed disodium, including pemetrexed ditromethamine. (Filing No. 74-1 at 36.) Lilly responds that pemetrexed ditromethamine was never disclosed in the specification of the

[6] Hospira agrees that there are no fact issues to resolve regarding its disclosure-dedication doctrine argument, and that the issue must be resolved on summary judgment. (Filing No. 79-3 at 11-12.)

'209 Patent, as an alternative or otherwise, and that Lilly prosecuted claims that encompassed pemetrexed ditromethamine. (Filing No. 79 at 31.)

"[W]hen a patent drafter discloses but declines to claim subject matter … this action dedicates that unclaimed subject matter to the public." *Johnson*, 285 F. 3d at 1054. "[T]he public notice function of patents suggests that before unclaimed subject matter is deemed to have been dedicated to the public, that unclaimed subject matter must have been identified by the patentee as an alternative to a claim limitation." *Pfizer Inc. v. Teva Pharmaceuticals, USA, Inc.*, 429 F.3d 1364 (Fed. Cir. 2005). Generic references in a written specification do not necessarily dedicate all members of a particular genus to the public. *SanDisk Corp. v. Kingston Technology Co., Inc.*, 695 F.3d 1348, 1363 (Fed. Cir. 2012).

> Rather, the 'disclosure must be of such specificity that one of ordinary skill in the art could identify the subject matter that had been disclosed and not claimed.' Additionally, in *Pfizer Inc. v. Teva Pharmaceuticals, USA, Inc.*, 429 F.3d 1364 (Fed. Cir. 2005), this court further clarified that 'before unclaimed subject matter is deemed to have been dedicated to the public, that unclaimed subject matter must have been identified by the patentee as an alternative to a claim limitation.'

Id. (citations omitted). It is undisputed that pemetrexed ditromethamine was not disclosed specifically in the '209 Patent, rather Hospira's disclosure-dedication argument hinges on Lilly's disclosure of "any antifolate". (Filing No. 74-1 at 35.) Additionally, Lilly asserts that pemetrexed ditromethamine is not an alternative to pemetrexed disodium, rather the two are the same antifolates because the active moiety—pemetrexed—targets the same relevant enzymes as defined in the '209 Patent specification and understood by a POSA. (Filing No. 79 at 32-33.) Because pemetrexed ditromethamine was not disclosed and identified with specificity, the disclosure-dedication rule does not prevent Lilly from pursuing a doctrine of equivalents infringement theory nor dedicated it to the public.

C. Inducement and Contribution to Infringement

Direct infringement occurs when one party makes, uses, offers to sell, sells, or imports each element of a patented invention. 35 U.S.C. § 271(a). Additionally, a party can be held liable for indirect infringement by actively inducing or contributing to direct infringement by others. 35 U.S.C. § 271(b), (c). "Inducement requires that the alleged infringer knowingly induced infringement and possessed a specific intent to encourage another's infringement." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1056 (Fed. Cir. 2010). Courts have inferred intent to induce infringement based on the contents of labels. *Id.* (holding circumstantial evidence may suffice to prove specific intent to induce infringement). "The pertinent question is whether the proposed label instructs users to perform the patented method. If so, the proposed label may provide evidence of [] affirmative intent to induce infringement." *AstraZeneca*, 633 F.3d at 1060. Similarly, labels may also form the basis to infer intent under contributory infringement when they instruct users to perform a patented method. *See Eli Lilly & Co. v. Actavis Elizabeth LLC*, 435 F. App'x 917, 926 (Fed. Cir. 2011). In a Hatch-Waxman case such as this, infringement "is focused on the product that is likely to be sold following FDA approval," including the relevant knowledge of the parties at the time the product is sold. *See Abbott Laboratories v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002) ("This determination is based on consideration of all the relevant evidence, including the ANDA filing, other materials submitted by the accused infringer to the FDA, and other evidence provided by the parties.").

Hospira concedes that its label directs the use of folic acid and vitamin B_{12} as set forth in the '209 Patent claims. (Filing No. 79-3 at 16.) Additionally, Hospira also concedes that should this Court find literal infringement of "pemetrexed disodium" or finds that there is no bar to infringement under the doctrine of equivalents, then, as a matter of law, use (and sale) of Hospira's NDA products according to their labeling, would satisfy indirect infringement under both

inducement and contributory theories. Moreover, Hospira has not addressed indirect infringement in its summary judgment brief. Because the Court has found Hospira's product literally infringes and that there is no bar to infringement under the doctrine of equivalents, summary judgment is **granted** to Lilly as to Hospira's inducement of and contribution to infringement of the '209 Patent.

IV. CONCLUSION

For the foregoing reasons, Hospira's Motion for Summary Judgment of Non-Infringement (Filing No. 73) is **DENIED** and Lilly's Cross-Motion for Summary Judgment of Infringement pursuant to literal infringement and doctrine of equivalents (Filing No. 78) is **GRANTED.**

SO ORDERED.

Date: 6/15/2018

TANYA WALTON PRATT, JUDGE
United States District Court
Southern District of Indiana

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