APPENDIX

TABLE OF APPENDICES

Appendix A

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

Nos. 18-2126, 18-2127

ELI LILLY AND COMPANY,
Plaintiff-Appellee,
v.
HOSPIRA, INC.,
Defendant-Appellant.

No. 2018-2128

ELI LILLY AND COMPANY,
Plaintiff-Appellee,
v.
DR. REDDY'S LABORATORIES, LTD., DR. REDDY'S LABORATORIES, INC.,
Defendants-Appellants.

Dated: August 9, 2019

Before: Lourie, Moore, and Taranto,
Circuit Judges.

OPINION

LOURIE, *Circuit Judge*:

Hospira Inc. ("Hospira"), Dr. Reddy's Laboratories Ltd., and Dr. Reddy's Laboratories Inc. (collectively, "DRL") appeal from two judgments of the United States District Court for the Southern District of Indiana in two infringement suits brought by Eli Lilly & Company ("Lilly") under the Hatch-Waxman Act, 21 U.S.C. § 355. The district court held in each case that the defendant's submission of a New Drug Application pursuant to 21 U.S.C. § 355(b)(2) infringed U.S. Patent 7,772,209 (the "'209 patent") under 35 U.S.C. § 271(e)(2). *See Eli Lilly & Co. v. Hospira, Inc.*, No. 1:16-cv-03460-TWP-MPB, 2018 WL 3008570 (S.D. Ind. June 15, 2018) ("*Hospira Decision*"); *Eli Lilly & Co. v. Dr. Reddy's Labs., Ltd.*, 323 F. Supp. 3d 1042 (S.D. Ind. 2018) ("*DRL Decision*"); *see also Eli Lilly & Co. v. Dr. Reddy's Labs., Ltd.*, No. 1:16-cv-00308-TWP-MPB, 2017 WL 6387316 (S.D. Ind. Dec. 14, 2017) ("*DRL Summary Judgment Decision*"). Accordingly, the district court entered orders under 35 U.S.C. § 271(e)(4)(A) prohibiting FDA approval of the products at issue until the expiration of the '209 patent. *Eli Lilly & Co. v. Hospira, Inc.*, No. 1:16-cv-03460-TWP-MPB (S.D. Ind. June 27, 2018), ECF No. 94; *Eli Lilly & Co. v. Dr. Reddy's Labs., Ltd.*, No. 1:16-cv-00308-TWP-MPB, 2018 WL 3616715 (S.D. Ind.

July 27, 2018). We decide these appeals together in this combined opinion.[1]

We reverse the district court's finding of literal infringement in the *Hospira Decision* as clearly erroneous in light of the court's claim construction of "administration of pemetrexed disodium." Because the district court did not err in its application of the doctrine of equivalents in either decision, we affirm both judgments of infringement. Thus, the *Hospira Decision* is affirmed-in-part and reversed-in-part, and the *DRL Decision* is affirmed.

Background

Lilly markets the compound pemetrexed in the form of a disodium salt as Alimta®, which is indicated, both alone and in combination with other active agents, for treating certain types of non-small cell lung cancer and mesothelioma. Pemetrexed is an antifolate, a class of molecules which, at the time of the invention in 2001, was "one of the most thoroughly studied classes of antineoplastic agents." '209 patent col. 1 ll. 19-20. Antifolates are structurally similar to folic acid and work by competitively binding to certain enzymes that use folic acid metabolites as cofactors in several steps of de novo nucleotide synthesis. *Id.* col. 1 ll. 40-41. Unlike folic acid, antifolates do not enable these synthetic steps, but instead inhibit them. Pemetrexed inhibits several of these enzymes, including thymidylate synthase, which methylates deoxyuridine in the final step of deoxythymidine

[1] We refer to the joint appendices in these appeals by reference to each appellant. Lilly's brief in the Hospira appeal is referred to as "Lilly Br. I" and its brief in the DRL appeal as "Lilly Br. II."

synthesis. *Id.* col. 1 ll. 59-61. By inhibiting the creation of these nucleotides, antifolates slow down DNA and RNA synthesis, and with it, cell growth and division. Cancer cells tend to grow rapidly, so antifolate therapy affects them disproportionately, but healthy cells can also be damaged.

Pemetrexed had been known for at least a decade in 2001. Lilly's U.S. Patent 5,344,932 ("Taylor") disclosed that certain glutamic acid derivatives with pyrrolo[2,3-d]pyrimidine heterocyclic ring structures, exemplified by pemetrexed, are "particularly active … inhibitors of thymidylate synth[ase]," Taylor col. 1 ll. 59-60; *see also id.* col. 19 l. 37-col. 20 l. 25 (disclosing data indicating that pemetrexed inhibits thymidylate synthase activity in vitro in human cell lines and in vivo in mice). The Taylor patent also disclosed that its compounds could be employed as "pharmaceutically acceptable salt[s]," *id.* col. 2 l. 35, and that the disodium salt form was particularly advantageous, *id.* col. 2 ll. 47-48. U.S. Patent 4,997,838 ("Akimoto"), to which Lilly took a license, disclosed a large genus of compounds containing pyrrolo[2,3-d]pyrimidine heterocyclic ring structures and a glutamic acid functional group, and that encompassed pemetrexed. The Akimoto patent discloses nearly fifty exemplary compounds, col. 14 l. 61-col. 16 l. 48, none of which is pemetrexed. Akimoto further discloses that its compounds may be prepared as salts of "pharmaceutically acceptable bases," such as "alkali metals, alkali earth metals, non-toxic metals, ammonium, and substituted ammonium." *Id.* col. 14 ll. 44-47.

By 2001, Lilly had also published the results of several clinical trials investigating the use of pemetrexed disodium as a treatment for different types of cancer. *See, e.g.*, W. John et al., "Activity of Multitargeted Antifolate (Pemetrexed Disodium, LY231514) in Patients with Advanced Colorectal Carcinoma: Results from a Phase II Study," *Cancer*, 88(8):1807-13 (2000). In the course of conducting these studies, Lilly discovered that pemetrexed disodium caused severe hematologic and immunologic side effects, resulting in infections, nausea, rashes, and even some deaths. *See id.*; *see also Neptune Generics, LLC v. Eli Lilly & Co.*, 921 F.3d 1372, 1377-78 (Fed. Cir. 2019) (discussing Lilly's response to adverse clinical data), *and Neptune Generics, LLC v. Eli Lilly & Co.*, No. IPR2016-00240, 2017 WL 4466557, at *28-30 (P.T.A.B. Oct. 5, 2017) (same). As the '209 patent teaches, such side effects are not uncommon among antifolates. *See* '209 patent col. 1 ll. 11-14. Some researchers hypothesized that folic acid deficiency caused these side effects and suggested supplementing pemetrexed disodium treatment with folic acid. DRL J.A. 7870 (citing J.F. Worzalla et al., "Role of Folic Acid in Modulating the Toxicity and Efficacy of the Multitargeted Antifolate, LY231514," *Anticancer Research*, 18:3235-40 (1998)).

The invention of the '209 patent is an improved method of treatment with antifolates, particularly pemetrexed disodium, through supplementation with a methylmalonic acid lowering agent and folic acid. Doing so, according to the patent, lessens antifolate toxicity without sacrificing efficacy. *See* '209 patent col. 10 ll. 17-53 (reporting that pre-supplementation regimen of vitamin B12 and folic acid in clinical

studies substantially reduced pemetrexed-induced toxicity and deaths while delivering a superior chemotherapeutic response rate). The '209 patent lists preferred antifolates, including some then-existing antifolate therapies, as well as "derivatives described in" several patents including the Akimoto patent, and "most preferred, Pemetrexed Disodium." *Id.* col. 4 ll. 28-43. Each of the claims of the '209 patent requires administration of pemetrexed disodium following administration of folic acid and a methylmalonic acid lowering agent, specified in some claims, as well as the Alimta® label, as vitamin B12. Claim 12 is representative[2]:

> 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 B12, prior to the first administration of pemetrexed disodium; and
>
> c) administration of pemetrexed disodium.

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[2] The district court treated claim 12 as representative, *DRL Summary Judgment Decision*, 2017 WL 6387316, at *1-2; *Hospira Decision*, 2018 WL 3008570, at *2, and no party has disputed that determination on appeal. *See, e.g.*, DRL Opening Br. 8-9; Hospira Opening Br. 23.

In a parent application, Application 10/297,821 (the "'821 application"), Lilly originally sought broad claims to methods of administering an antifolate in conjunction with a methylmalonic acid lowering agent, with or without folic acid. The original independent claims 2 and 5 read:

> 2. (Original) A method of reducing the toxicity associated with the administration of an antifolate to a mammal comprising
>
> > administering to said mammal an effective amount of said antifolate in combination with a methylmalonic acid lowering agent.
>
> 5. (Original) A method of reducing the toxicity associated with the administration of an antifolate to a mammal comprising
>
> > administering to said mammal an effective amount of said antifolate in combination with a methylmalonic acid lowering agent and FBP binding agent.

DRL J.A. 7860. A dependent claim further limited the an-tifolate to pemetrexed disodium. *Id.* at 7861.

Claim 2 was rejected as anticipated by F.G. Arsenyan et al., "Influence of Methylcobalamin on the Antineoplastic Activity of Methotrexate," *Onkol. Nauchn.*, 12(10):1299-1303 (1978), which disclosed experiments treating mice with various tumors with a combination of methotrexate, an antifolate, and methylcobalamin, a vitamin B12 derivative. The rest of the pending claims, including Claim 5, were rejected as obvious over a collection of references: U.S. Patent 5,431,925 ("Ohmori")—which taught treatment of

chemotherapeutically-induced immunosuppression with a combination of vitamins that could include folic acid and vitamin B12—Worzalla, John, and Arsenyan. '821 application, Sept. 27, 2004, Office Action; DRL J.A. 7868-72.

In response, Lilly amended both claims to narrow "antifolate" to "pemetrexed disodium" and cancelled its dependent claim limited to pemetrexed disodium. '821 application, Jan. 25, 2005, Response to Office Action; DRL J.A. 7877-84. In its remarks, Lilly asserted that the amendment to claim 2 overcame the anticipation rejection because Arsenyan does not disclose pemetrexed disodium. *Id*. To overcome the obviousness rejection of claim 5 and its dependents, Lilly generally argued that, while John discloses hematologic and immunologic toxicities from administration of pemetrexed disodium, it never suggests vitamin supplementation, and none of the other references "teach the use of [vitamin B12] to reduce toxicities associated with an antifolate." *Id.* The examiner then withdrew the anticipation rejection and later withdrew the obviousness rejection. The '821 application issued as U.S. Patent 7,053,065, and the '209 patent later issued from a continuation application.

These appeals were taken from cases which are among the latest in a series of patent disputes about Alimta® that reaches back more than a decade.[3] In

[3] This is the fourth appeal we have decided concerning Alimta® and the third specifically concerning the '209 patent. *See Neptune Generics*, 921 F.3d 1372; *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357 (Fed. Cir. 2017); *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 689 F.3d 1368 (Fed. Cir. 2012).

this most recent chapter, DRL, Hospira, and Actavis[4] submitted New Drug Applications under § 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(b)(2), relying on Lilly's clinical data for pemetrexed disodium. But each applicant seeks to market different pemetrexed salts—in DRL's and Hospira's applications, pemetrexed ditromethamine. Both DRL and Hospira represented to the FDA that their choice of the tromethamine cation was immaterial because pemetrexed dissociates from its counterion in solution, DRL J.A. 8555-57; Hospira J.A. 124, and tromethamine was known to be safe for pharmaceutical use, DRL J.A. 8555, 8557.

Lilly then asserted the '209 patent against each of these NDA applicants in the United States District Court for the Southern District of Indiana. In the DRL case, the district court construed the phrase "administration of pemetrexed disodium" to mean "liquid administration of pemetrexed disodium," which "is accomplished by dissolving the solid compound pemetrexed disodium into solution." *DRL Summary Judgment Decision*, 2017 WL 6387316, at *4. The district court denied DRL's motion for summary judgment of noninfringement, holding that prosecution history estoppel does not bar Lilly from

[4] Lilly also sued Actavis LLC ("Actavis") for infringement of the '209 patent, *Eli Lilly & Co. v. Actavis LLC*, No. 1:17-cv-00982-TWP-MPB (S.D. Ind. Mar. 30, 2017), ECF No. 1, but the parties stipulated to be bound by the district court's decision in the DRL case that neither prosecution history estoppel nor the disclosure-dedication rule bars Lilly's assertion of infringement through the doctrine of equivalents. Actavis Br. 2. Actavis filed a brief in the DRL appeal as amicus curiae requesting reversal of that portion of the district court's decision.

asserting that DRL's proposed pemetrexed ditromethamine product would infringe through the doctrine of equivalents because the reason for Lilly's amendment was to distinguish other antifolates and was therefore only tangential to pemetrexed ditromethamine. *Id.* at *6-7. The district court also rejected DRL's argument that Lilly dedicated pemetrexed ditromethamine to the public under the disclosure-dedication rule through its reference to Akimoto's antifolate compounds because Akimoto is not incorporated by reference into the '209 patent and in any event discloses pemetrexed ditromethamine only within a genus of thousands of compounds, which the district court held does not constitute the requisite disclosure of an identifiable alternative under this court's precedent. *Id.* at *7-8; *see, e.g.*, *SanDisk Corp. v. Kingston Tech. Co.*, 695 F.3d 1348, 1363 (Fed. Cir. 2012).

Following a bench trial, the district court's opinion largely followed its rationale in the *DRL Summary Judgment Decision* with respect to the applicability of prosecution history estoppel and the disclosure-dedication rule. *DRL Decision*, 323 F. Supp. 3d at 1046-48. In addition, the court found that DRL's proposed product would be administered in a manner that would meet the "administration of pemetrexed disodium" step of the asserted claims under the doctrine of equivalents, *id.* at 1049, regardless of the "differences in chemical properties between pemetrexed disodium and pemetrexed ditromethamine," *id.* at 1050.

In the Hospira case, the parties similarly disputed the doctrine of equivalents, but Lilly also asserted

literal infringement because Hospira's proposed product label allows reconstitution of its pemetrexed ditromethamine salt in saline. *Hospira Decision*, 2018 WL 3008570, at *2-3; Hospira J.A. 229. After the district court issued the *DRL Summary Judgment Decision*, Hospira conceded, contingent upon its right to appeal, that its product would infringe under the claim construction of "administration of pemetrexed disodium" set forth in that opinion and that its doctrine of equivalents arguments were likewise foreclosed. Hospira Br. 18. The district court, "rel[ying] heavily" on the *DRL Summary Judgment Decision*, granted Lilly's motion for summary judgment of infringement, both literally and under the doctrine of equivalents. *Hospira Decision*, 2018 WL 3008570, at *1 n.2, *6.

These appeals followed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

We review a district court's grant of summary judgment according to the law of the regional circuit. *Kaneka Corp. v. Xiamen Kingdomway Grp. Co.*, 790 F.3d 1298, 1303 (Fed. Cir. 2015) (citing *Halo Elecs., Inc. v. Pulse Elecs., Inc.*, 769 F.3d 1371, 1377 (Fed. Cir. 2014)). In the Seventh Circuit, summary judgment is reviewed *de novo*, construing all facts and drawing all inferences in favor of the non-movant. *Wis. Alumni Research Found. v. Apple Inc.*, 905 F.3d 1341, 1352 (Fed. Cir. 2018) (citing *Austin v. Walgreen Co.*, 885 F.3d 1085, 1087 (7th Cir. 2018)). On appeal from a bench trial, we review a district court's conclusions of law *de novo* and its findings of fact for clear error. *Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d

1349, 1358 (Fed. Cir. 2014) (citing *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1123 (Fed. Cir. 2000)). A factual finding is clearly erroneous if, despite some supporting evidence, we are left with the definite and firm conviction that a mistake has been made. *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 395 (1948).

Claim construction is ultimately an issue of law, which we review *de novo*. *Shire Dev., LLC v. Watson Pharm., Inc.*, 787 F.3d 1359, 1364 (Fed. Cir. 2015). We review *de novo* the district court's findings of fact on evidence "intrinsic to the patent (the patent claims and specification[], along with the patent's prosecution history)," and review for clear error extrinsic findings of fact. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 841 (2015). While infringement is a question of fact, *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1309 (Fed. Cir. 2009), we review *de novo* the district court's grant of summary judgment of non-infringement, *Unwired Planet, LLC v. Apple Inc.*, 829 F.3d 1353, 1356 (Fed. Cir. 2016). To prove infringement, a patentee "must supply sufficient evidence to prove that the accused product or process contains, either literally or under the doctrine of equivalents, every limitation of the properly construed claim." *Seal-Flex, Inc. v. Athletic Track & Court Const.*, 172 F.3d 836, 842 (Fed. Cir. 1999). The patentee has the burden of proving infringement by a preponderance of the evidence. *SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988).

Hospira requests reversal of the district court's finding that its submission of a § 505(b)(2) NDA for its

pemetrexed product literally infringed the claims of the '209 patent. DRL and Hospira both argue, as does the amicus curiae Actavis, that the district court erred as a matter of law by refusing to apply prosecution history estoppel to bar Lilly's doctrine of equivalents claim, and DRL further contends that the disclosure-dedication rule precludes Lilly's equivalents claim. Finally, DRL disputes the district court's finding that administration of pemetrexed ditromethamine is equivalent to the claim element "administration of pemetrexed disodium." We address each argument in turn.

A. Literal Infringement

Hospira argues that it cannot literally infringe the claims of the '209 patent because intravenous administration of pemetrexed ditromethamine dissolved in saline—a solution which contains pemetrexed and chloride anions alongside sodium and tromethamine cations—is not "administration of pemetrexed disodium." Hospira also notes that such a solution will, in any case, contain far more than two sodium cations per pemetrexed anion. Finally, Hospira appears to make a perfunctory argument that, in the alternative, we should reverse the district court's construction and hold that the term encompasses any route of administering pemetrexed disodium, not just liquid, as the district court's construction requires.

Lilly counters that Hospira's view improperly imposes a "source limitation," requiring that the pemetrexed disodium salt exist in solid form before administration, even though Hospira's proposed product label, like that of Alimta®, calls for

administration of a solution containing pemetrexed anions and sodium cations. Lilly also contends that Hospira's claim construction arguments are irrelevant because Hospira's proposed product will be administered intravenously anyway.

We agree with Hospira. It was clearly erroneous for the district court to hold that the "administration of pemetrexed disodium" step was met because Hospira's pemetrexed ditromethamine product will be dissolved in saline before administration. A solution of pemetrexed and chloride anions and tromethamine and sodium cations cannot be deemed pemetrexed disodium simply because some assortment of the ions in the solution consists of pemetrexed and two sodium cations. As Lilly acknowledges throughout its brief, pemetrexed disodium is a salt. *See, e.g.*, Lilly Br. I 12 (pemetrexed toxicity is caused "by pemetrexed itself once dissociated in solution," not pemetrexed disodium); *see also* Hospira J.A. 1596 (October 2017 Alimta® Label referring to the drug substance as the "disodium salt" of pemetrexed). Once diluted, the salt's crystalline structure dissolves, and the individual ions dissociate. *See* Hospira J.A. 2820 (declaration of Lilly's expert). In other words, pemetrexed disodium no longer exists once dissolved in solution, and, as a corollary, a different salt of pemetrexed dissolved in saline is not pemetrexed disodium.

We conclude that to literally practice the "administration of pemetrexed disodium" step under the district court's claim construction, the pemetrexed disodium salt must be itself administered. *See DRL Summary Judgment Decision*, 2017 WL 6387316, at *4 ("'[A]dministration of pemetrexed

disodium' … refer[s] to a liquid administration of pemetrexed disodium. … , accomplished by dissolving the solid compound pemetrexed disodium into solution ….”); *see also Tex. Instruments Inc. v. Cypress Semiconductor Corp.*, 90 F.3d 1558, 1563 (Fed. Cir. 1996) (“To literally infringe, the accused … process must contain every limitation of the asserted claim.” (citing *Laitram Corp. v. Rexnord, Inc.*, 939 F.2d 1533, 1535 (Fed. Cir. 1991))). There is no dispute that Hospira has only sought approval to market pemetrexed ditromethamine, Lilly Br. I 4, and that neither its proposed product nor methods of administering it will constitute administering the pemetrexed disodium salt. Accordingly, Hospira will not practice the step of “administration of pemetrexed disodium,” and the district court's finding of literal infringement must be reversed.

B. Doctrine of Equivalents

Few propositions of patent law have been so consistently sustained by the Supreme Court as the doctrine of equivalents. *See Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushki Co.*, 535 U.S. 722, 733 (2002) (“*Festo VIII*”) (“[E]quivalents remain a firmly entrenched part of the settled rights protected by the patent.”); *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 40 (1997) (“[W]e adhere to the doctrine of equivalents.”); *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608 (1950) (“Originating almost a century ago in the case of *Winans v. Denmead*, [56 U.S. 330 (1853)] … [the doctrine of equivalents] has been consistently applied by this Court and the lower federal courts, and continues today ready and available for utilization

when the proper circumstances for its application arise."). It is settled that a patentee is entitled "in all cases to invoke to some extent the doctrine of equivalents," *Seymour v. Osborne*, 78 U.S. 516, 555 (1870), without a "judicial exploration of the equities of a case" beforehand. *See Warner-Jenkinson*, 520 U.S. at 34.

Yet the Supreme Court has also acknowledged that the doctrine of equivalents, "when applied broadly, conflicts with the definitional and public-notice functions of the statutory claiming requirement," *Warner-Jenkinson*, 520 U.S. at 29, and that, without the proper balance between these two imperatives, the doctrine may "take[] on a life of its own, unbounded by the patent claims." *See id.* at 28-29. We have emphasized, moreover, that the doctrine of equivalents is "the exception, however, not the rule," and not merely "the second prong of every infringement charge, regularly available to extend protection beyond the scope of the claims." *London v. Carson Pirie Scott & Co.*, 946 F.2d 1534, 1538 (Fed. Cir. 1991). Patent infringement is principally determined by examining whether the accused subject matter falls within the scope of the claims.

To that end, courts have placed important limitations on a patentee's ability to assert infringement under the doctrine of equivalents. *See, e.g.*, *Festo VIII*, 535 U.S. at 737-41 (prosecution history estoppel); *Warner-Jenkinson*, 520 U.S. at 39 n.8 ("[A] theory of equivalence [cannot] entirely vitiate a particular claim element …."); *Graver Tank*, 339 U.S. at 608 (accused equivalent cannot differ substantially from the claimed invention); *Johnson & Johnston*

Assocs. Inc. v. R.E. Serv. Co., 285 F.3d 1046, 1054 (Fed. Cir. 2002) (en banc) (subject matter disclosed but not claimed is dedicated to the public) (citing *Maxwell v. J. Baker, Inc.*, 86 F.3d 1098 (Fed. Cir. 1996)); *Wilson Sporting Goods Co. v. David Geoffrey & Assocs.*, 904 F.2d 677, 683 (Fed. Cir. 1990) ("[T]he asserted scope of equivalency [cannot] encompass the prior art ...." (Rich, J.) (citations omitted)). These appeals implicate several of these limitations.

1. Prosecution History Estoppel

The main dispute in these appeals is whether Lilly has rebutted the presumption of prosecution history estoppel that attached to its amendment in the '821 application. Prosecution history estoppel arises when a patent applicant narrows the scope of his claims during prosecution for a reason "substantial[ly] relating to patentability." *See generally Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1366-67 (Fed. Cir. 2003) (en banc) ("*Festo X*"). Such a narrowing amendment is presumed to be a surrender of all equivalents within "the territory between the original claim and the amended claim," but the presumption is overcome if the patentee can show the applicability of one of the few exceptions identified by the Supreme Court. *Festo VIII*, 535 U.S. at 740-41 (citing *Exhibit Supply Co. v. Ace Patents Corp.*, 315 U.S. 126, 136-37 (1942)). Whether prosecution history estoppel applies to bar a doctrine of equivalents claim is a question of law, reviewed *de novo*. *See Regents of Univ. of Cal. v. Dakocytomation Cal., Inc.*, 517 F.3d 1364, 1371 (Fed. Cir. 2008) (citing *Pharmacia & Upjohn Co. v. Mylan Pharm., Inc.*, 170 F.3d 1373, 1376 (Fed. Cir. 1999)).

Lilly does not dispute that the amendment in question was both narrowing and made for a substantial reason relating to patentability. Lilly Br. II 21. Furthermore, Lilly relies on only one exception to giving effect to the presumption as to the scope of surrender: that the rationale of its amendment "[bore] no more than a tangential relation to the equivalent in question." *Festo VIII*, 535 U.S. at 740. As a result, the parties' dispute about whether prosecution history estoppel applies is confined to whether Lilly's amendment narrowing "an antifolate" to "pemetrexed disodium" was only tangential to pemetrexed ditromethamine, which is the accused compound. Whether the tangential exception applies is a question of law, *Integrated Tech. Corp. v. Rudolph Techs., Inc.*, 734 F.3d 1352, 1356 (Fed. Cir. 2013), and a patentee seeking to use the exception "must base his arguments solely upon the public record of the patent's prosecution." *Festo X*, 344 F.3d at 1369-70 (citation omitted).

The Appellants argue that Lilly failed to explain why it did not pursue a narrower amendment literally encompassing pemetrexed ditromethamine, and they emphasize our statement that the tangential exception is "very narrow." *Integrated*, 734 F.3d at 1358 (quoting *Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.*, 480 F.3d 1335, 1342 (Fed. Cir. 2007)). The Appellants further point out that Lilly cannot be said to have "lacked the words to describe" pemetrexed ditromethamine, *see Festo VIII*, 535 U.S. at 734, because Lilly's previous patents, as well as the European companion to the '209 patent, claimed pemetrexed salts generally and pemetrexed disodium in a dependent claim. They also assert that the district

court erred by focusing on whether Lilly actually needed to relinquish pemetrexed ditromethamine to overcome the Arsenyan anticipation rejection because "the tangential exception is not a patentee's-buyer's-remorse exception." DRL Br. 39.

In response, Lilly argues that the district court properly held that the reason for its amendment was to distinguish pemetrexed from antifolates generally and that the different salt type is a merely tangential change with no consequence for pemetrexed's administration or mechanism of action within the body. Lilly also contends that it is not barred from asserting the tangential exception simply because pemetrexed ditromethamine is within "the territory between the original claim and the amended claim." *Festo VIII*, 535 U.S. at 740. Finally, Lilly argues that Appellants' view that courts must "consider hypothetical alternative amendments" that would literally encompass the alleged equivalent "would eviscerate the tangentiality exception." Lilly Br. II 44.

We agree with Lilly. As a general matter, we find Appellants' view of prosecution history estoppel, and the tangential exception in particular, too rigid. Tangential means "touching lightly or in the most tenuous way." Webster's Third New International Dictionary (2002). The reason for Lilly's amendment, as the district court concluded, was to narrow original claim 2 to avoid Arsenyan, which only discloses treatments using methotrexate, a different antifolate. *See* DRL J.A. 7879-80 (overcoming the Arsenyan anticipation rejection by arguing that it "does not disclose pemetrexed disodium"). To overcome a clear anticipation, Lilly opted to narrow its original claim 2

and its dependents to more accurately define what it actually invented, an improved method of administering pemetrexed. In other words, the particular type of salt to which pemetrexed is complexed relates only tenuously to the reason for the narrowing amendment, which was to avoid Arsenyan. We therefore hold that Lilly's amendment was merely tangential to pemetrexed ditromethamine because the prosecution history, in view of the '209 patent itself, strongly indicates that the reason for the amendment was not to cede other, functionally identical, pemetrexed salts.

The prosecution record confirms our understanding. Original claim 5, which, like all the current claims of the '209 patent, required supplementation with both vitamin B12 and folic acid, was never rejected as anticipated over Arsenyan. Instead, the art cited against original claim 5 and its dependent claims in the obviousness ground of rejection was replete with information about pemetrexed disodium; John disclosed clinical trials using pemetrexed disodium, reporting both its efficacy and its toxic side effects, and in response, DRL J.A. 7869-70, Worzalla suggested folic acid supplementation to counteract these side effects, DRL J.A. 7870-71. The prosecution record implies that Lilly's amendment, inartful though it might have been, was prudential in nature and did not need or intend to cede other pemetrexed salts.

Hospira argues that the amendment was made to overcome the obviousness rejection over Ohmori and John and that Lilly has provided no reason for the amendment relative to that rejection. Like Lilly, we

find this argument makes little sense. John discloses the results of a clinical trial of pemetrexed disodium and explicitly suggests the toxicities caused by pemetrexed; as we concluded above, narrowing "antifolate" to "pemetrexed disodium" could not possibly distinguish the art cited in the obviousness ground of rejection.

DRL also insists that we have held that an applicant's remorse at ceding more claim scope than necessary is not a reason for the tangential exception to apply. *See, e.g.*, *Lucent Techs., Inc. v. Gateway, Inc.*, 525 F.3d 1200, 1218 (Fed. Cir. 2008); *Schwarz Pharma, Inc. v. Paddock Labs., Inc.*, 504 F.3d 1371, 1377 (Fed. Cir. 2007). This is generally true, but DRL overreads the holdings of these cases. After all, the tangential exception only exists because applicants over-narrow their claims during prosecution. Amendments are not construed to cede only that which is necessary to overcome the prior art, *see Schwarz*, 504 F.3d at 1377, nor will the court "speculat[e]" whether an amendment was necessary, *see Kinzenbaw v. Deere & Co.*, 741 F.2d 383, 389 (Fed. Cir. 1984). But the reason for an amendment, where the tangential exception is invoked, cannot be determined without reference to the context in which it was made, including the prior art that might have given rise to the amendment in the first place. *See Festo X*, 344 F.3d at 1370. Here, it is unlikely that a competitor would have been "justified in assuming that if he [made an equivalent pemetrexed salt], he would not infringe [the '209 patent]." *Kinzenbaw*, 741 F.2d at 389; *cf. Festo VIII*, 535 U.S. at 738 ("There is no reason why a narrowing amendment should be

deemed to relinquish equivalents … beyond a fair interpretation of what was surrendered.").

Furthermore, Appellants' suggestion that Lilly must prove that it could not have drafted a claim that literally encompassed pemetrexed ditromethamine is unsupported by our precedent on prosecution history estoppel, not to mention excessive. We do not demand perfection from patent prosecutors, and neither does the Supreme Court. *See Festo VIII*, 535 U.S. at 738 ("It does not follow … that [an] amended claim becomes so perfect in its description that no one could devise an equivalent."). Lilly's burden was to show that pemetrexed ditromethamine was "peripheral, or not directly relevant," to its amendment, *Festo X*, 344 F.3d at 1369. And as we concluded above, Lilly has done so.

In addition, the Appellants maintain that when a patentee submits an amendment adding two claim limitations, it cannot later argue that the reason for the amendment was tangential to an accused equivalent containing only one of the added limitations simply because the second limitation was unnecessary to overcome the prior art. They offer *Felix v. American Honda Motor Co.*, 562 F.3d 1167 (Fed. Cir. 2009), as an illustration of this principle.[5] In that case,

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[5] The parties argue at length about which of our cases are properly analogous to the facts presented in these appeals. Here, in applying the Supreme Court's framework, we find the analogies to other cases less helpful than a direct consideration of the specific record of this case and what it shows about the reason for amendment and the relation of that reason to the asserted equivalent. This case-specific focus, within the governing framework, comports with the equitable nature of prosecution history estoppel. *See Festo VIII*, 535 U.S. at 738 ("[The Supreme Court has] consistently applied the doctrine in a

we held that prosecution history estoppel applied to a claim directed to a vehicle bed storage system—limited in response to a rejection to having a channel with a flange and a gasket mounted on that flange—barring assertion of equivalence with respect to a product that met the channel aspect, but not the gasket aspect, of the limitation. *Id.* at 1184-85.

But as Lilly points out, this holding was determined by that patent's prosecution history, *Felix*, 562 F.3d at 1184, and we have also held that prosecution history estoppel does not apply in similar circumstances, where the prosecution record differed. *See, e.g.*, *Regents*, 517 F.3d at 1376-78 (amendment narrowing "disabling hybridization capacity of [nucleic acid] sequences" to methods using a "blocking nucleic acid" was merely tangential to unclaimed repetitive sequence nucleic acids); *Insituform Techs., Inc. v. CAT Contracting, Inc.*, 385 F.3d 1360, 1368 (Fed. Cir. 2004) (amendment narrowing method of inserting resin into tube using a vacuum to one using "a cup" to do so was merely tangential to a multiple cup embodiment because the number of cups bore no relationship to the cited prior art or the rationale behind the narrowing amendment). Thus, our cases demonstrate that prosecution history estoppel is resistant to the rigid legal formulae that Appellants seek to extract from them. *See Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1291 (Fed. Cir. 2010) ("[T]here is

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flexible way, not a rigid one."); *cf. Heckler v. Cmty. Health Servs. of Crawford Cty., Inc.*, 467 U.S. 51, 59 (1984) ("Estoppel is an equitable doctrine invoked to avoid injustice in particular cases.… [and] a hallmark of the doctrine is its flexible application ….").

no hard-and-fast test for what is and what is not a tangential relation ….").

Finally, DRL also contends that our precedent squarely forecloses Lilly's tangentiality argument, and it invites us to read those cases to hold that "where the reason for the amendment and the equivalent in question both relate to the same claim element, the tangential exception does not apply." DRL Br. 47. We decline this invitation because such a bright-line rule is both contrary to the equitable nature of prosecution history estoppel, as articulated in *Festo VIII*, 535 U.S. at 738, and inconsistent with the equitable spirit that animates the doctrine of equivalents, *see Graver Tank*, 339 U.S. at 608-09 (the doctrine is one of "wholesome realism"). Instead, we reaffirm that whether an amendment was merely tangential to an equivalent must be decided in the context of the invention disclosed in the patent and the prosecution history. *Festo X*, 344 F.3d at 1370.

DRL's intuition—that an amendment that narrows an existing claim element evinces an intention to relinquish that claim scope—is often correct. Indeed, as we have found in previous cases, it is a powerful indication that an amendment was not merely tangential. *See, e.g.*, *Honeywell Int'l, Inc. v. Hamilton Sundstrand Corp.*, 523 F.3d 1304, 1315-16 (Fed. Cir. 2008); *Biagro W. Sales, Inc. v. Grow More, Inc.*, 423 F.3d 1296, 1306 (Fed. Cir. 2005). But here, we conclude that this consideration is not dispositive because the rest of the prosecution history, and the '209 patent itself, show that it is implausible that the reason for Lilly's amendment was to surrender other pemetrexed salts. Indeed, such a relinquishment

would effectively dedicate the entirety of Lilly's invention to the public and thereby render the '209 patent worthless, and it would have been irrelevant for distinguishing the prior art. Again, the prosecution history strongly indicates a less sweeping and more sensible reason for Lilly's amendment: to surrender antifolates other than pemetrexed. Thus, we conclude on this prosecution record that Lilly's amendment was merely tangential to pemetrexed ditromethamine.

2. Disclosure-Dedication Rule

DRL next argues that the disclosure-dedication rule bars Lilly from asserting infringement under the doctrine of equivalents. The '209 patent sets forth its invention as an improved method of administering antifolates, '209 patent col. 2 ll. 47-58, and teaches that the derivatives described in the Akimoto patent are preferred examples of antifolates, *id.* col. 4 ll. 34-40. DRL contends that one of these derivatives is pemetrexed ditromethamine and that it was dedicated to the public when Lilly declined to claim it. DRL asserts that the district court erred because it both required express incorporation of Akimoto by reference into the '209 patent and concluded that Akimoto does not specifically disclose pemetrexed ditromethamine.

Lilly counters that the disclosure-dedication rule requires express disclosure of the subject matter in question in the specification except in narrow circumstances, such as when that subject matter is disclosed in a priority application, *see Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1297 (Fed. Cir. 2009), or prior art expressly incorporated by reference, *SanDisk*, 695 F.3d at 1366. Lilly also argues that the

district court correctly determined that the relevant portion of Akimoto discloses only a generic formula from which a skilled artisan would not be able to recognize pemetrexed ditromethamine.

We agree with Lilly and hold that the disclosure-dedication rule is inapplicable to this case because the '209 patent does not disclose methods of treatment using pemetrexed ditromethamine, and, as a result, Lilly could not have dedicated such a method to the public.

Under the disclosure-dedication rule, subject matter disclosed by a patentee, but not claimed, is considered dedicated to the public. *See Johnson & Johnston*, 285 F.3d at 1054. The reason for the doctrine is that members of the public reading a disclosure of particular subject matter are entitled, absent a claim to it, to assume that it is not patented and therefore dedicated to the public (unless, for example, claimed in a continuation or other application based on the disclosure). *Cf. Maxwell*, 86 F.3d at 1107 (failure to claim inventive subject matter "is clearly contrary to 35 U.S.C. § 112, which requires that a patent applicant 'particularly point[] out and distinctly claim[] the subject matter which the applicant regards as his invention'"). Subject matter is considered disclosed when a skilled artisan "can understand the unclaimed disclosed teaching upon reading the written description," but not "any generic reference … necessarily dedicates all members of that particular genus." *PSC Comput. Prod., Inc. v. Foxconn Int'l, Inc.*, 355 F.3d 1353, 1360 (Fed. Cir. 2004).

DRL further contends that the disclosure-dedication rule does not impose a § 112 requirement

for sufficiency of disclosure, *see Toro Co. v. White Consol. Indus., Inc.*, 383 F.3d 1326, 1334 (Fed. Cir. 2004), and that a skilled artisan reading the '209 patent would both look for a disclosure of pemetrexed in Akimoto, and also seek to use a well-known cation like tromethamine, which it maintains is generically disclosed in Akimoto in the form of "substituted ammonium" base salts.

We are unpersuaded by DRL's arguments. As the district court noted, Akimoto's formula, col. 1 l. 49-col. 2 l. 3, includes seven functional group variables and encompasses thousands of compounds, and while Akimoto discloses about fifty exemplary compounds, none of them is pemetrexed. Moreover, Akimoto does not even disclose tromethamine expressly but only generically among dozens of other salts. At most, Akimoto discloses ammonium salts generally, which is far from a description of tromethamine. In similar circumstances, we have held that "sufficient description of a genus" requires that a skilled artisan be able to "'visualize or recognize' the members of the genus." *See Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010) (quoting *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568-69 (Fed. Cir. 1997)). Akimoto does not so describe pemetrexed ditromethamine, and we see no reason why a skilled artisan would set out on DRL's winding path to cobble together pemetrexed ditromethamine. While the '209 patent teaches that pemetrexed disodium is the "most preferred" antifolate, that knowledge would not change the skilled artisan's understanding of what Akimoto discloses.

Because Akimoto contains only a "generic reference" to pemetrexed ditromethamine, *PSC Comput.*, 355 F.3d at 1360, we conclude that it was not dedicated to the public.

3. Merits

A component in an accused product or process may be equivalent to a claim element if the two are insubstantially different with respect to the "role played by [the] element in the context of the specific patent claim." *Warner-Jenkinson*, 520 U.S. at 39-40. Relevant differences can include the function each serves, the way in which each works, and the result each obtains, *id.* at 39, and, especially in biochemical cases, structural or pharmacological characteristics, *Mylan Inst. LLC v. Aurobindo Pharm. Ltd.*, 857 F.3d 858, 869 (Fed. Cir. 2017). "The determination of equivalency *vel non* is a question of fact," *Canton Bio Med., Inc. v. Integrated Liner Techs., Inc.*, 216 F.3d 1367, 1369 (Fed. Cir. 2000) (citing *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1218 (Fed. Cir. 1995)), which we review for clear error in an appeal from a bench trial, *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1359 (Fed. Cir. 2007).

DRL argues that the district court erred in finding that its proposed pemetrexed ditromethamine product will be administered in an insubstantially different way from the claimed method. DRL maintains that the district court focused on the fact that each product treats the same diseases by delivering pemetrexed intravenously, when the relevant context is the manner of administration. In DRL's view, the chemical differences between sodium and tromethamine—*e.g.*, pH, buffering capacity, or

solubility—DRL Br. 20-21, render the methods in which each is administered to a patient substantially different.

Lilly responds that the relevant context is treatment of a patient "in need of chemotherapeutic treatment." '209 patent claim 12. Lilly agrees with the district court that the chemical differences between sodium and tromethamine are clinically irrelevant because each undisputedly lacks therapeutic activity.

We see no clear error in the district court's findings. As the district court found, DRL's product will accomplish an identical aim, furnishing the same amount of pemetrexed to active sites in the body; in exactly the same way, by diluting a pemetrexed salt in an aqueous solution for intravenous administration. Indeed, after dilution and immediately before administration, DRL's product is functionally identical to Lilly's in that it contains the same amount of diluted pemetrexed anion. DRL J.A. 8557. And DRL declines to identify the relevance of any of the chemical differences it identifies. *See UCB, Inc. v. Watson Labs. Inc.*, 927 F.3d 1272, 1284-86 (Fed. Cir. 2019) (chemical differences may not be relevant if the equivalent has known interchangeability in the context of the claimed composition). We find DRL's arguments unconvincing and therefore affirm the district court's findings.

In summary, these cases are eminently suitable for application of the doctrine of equivalents, and we conclude that neither prosecution history estoppel nor the disclosure-dedication rule bars Lilly from asserting infringement through equivalence.

CONCLUSION

We have fully considered each party's further arguments but find them unpersuasive. For the foregoing reasons, we reverse the district court's finding of literal infringement in the *Hospira Decision* but affirm its judgment of infringement under the doctrine of equivalents. The judgment of infringement under the doctrine of equivalents in the *DRL Decision* is likewise affirmed.

AFFIRMED-IN-PART AND REVERSED-IN-PART IN APPEAL NOS. 2018-2126, 2018-2127

AFFIRMED IN APPEAL NO. 2018-2128

COSTS

Each party shall bear its own costs.

Appendix B

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

No. 18-2128

ELI LILLY AND COMPANY,

Plaintiff-Appellee,

v.

DR. REDDY'S LABORATORIES, LTD., DR. REDDY'S LABORATORIES, INC.,

Defendants-Appellants.

Dated: November 8, 2019

Before: Prost, *Chief Judge*, Newman, Lourie, Dyk, Moore, O'Malley, Reyna, Wallach, Taranto, Chen, Hughes, and Stoll, *Circuit Judges*.

Per Curiam.

ORDER

Appellants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. filed a petition for rehearing en banc. A response to the petition was invited by the court and filed by Appellee Eli Lilly and Company. The petition was first referred as a petition for rehearing to the panel that heard the appeal, and thereafter the petition for rehearing en banc was

referred to the circuit judges who are in regular active service.

Upon consideration thereof,

It is ordered that:

The petition for panel rehearing is denied.

The petition for rehearing en banc is denied.

The mandate of the court will issue on November 15, 2019.

FOR THE COURT

November 8, 2019
Date

Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court

Appendix C

UNITED STATES DISTRICT COURT FOR THE SOUTHERN DISTRICT OF INDIANA

No. 1:16-cv-00308-TWP-MPB

ELI LILLY AND COMPANY,

Plaintiff,

v.

DR. REDDY'S LABORATORIES, LTD., and DR. REDDY'S LABORATORIES, INC.,

Defendants.

Dated: June 22, 2018

FINDINGS OF FACT AND CONCLUSIONS OF LAW FOLLOWING FEBRUARY 1, 2018 BENCH TRIAL

This matter was before the Court for a bench trial beginning on February 1, 2018 and concluding on February 2, 2018, on the issue of infringement of U.S. Patent No. 7,772,209 (the "'209 Patent"). This is a Hatch-Waxman patent infringement action brought by Eli Lilly and Company ("Lilly"), the owner of the '209 Patent, against Defendants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. (collectively, "Dr. Reddy's") arising out of Dr. Reddy's filing of New Drug Application No. 208297 (the "NDA") with the Food and Drug Administration ("FDA") seeking approval to market the product

described therein. The '209 Patent describes a method of administering a chemotherapy drug, pemetrexed disodium ("pemetrexed"), with vitamins, which is marketed by Lilly under the trade name ALITMA®. Lilly is asserting that Dr. Reddy's drug product, which uses pemetrexed ditromethamine, infringes the '209 Patent. Dr. Reddy's contends that its product is not a generic drug, rather, its product uses a different chemical. Particularly at issue is claim 12. The Court previously constructed claim 12 to refer to a liquid administration of pemetrexed disodium. (Filing No. 199 at 9.) Having heard testimony and considered the exhibits and arguments of the parties, the Court makes the following findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52.

I. Findings of Fact

Lilly is a corporation organized and existing under the laws of the State of Indiana, having its corporate offices and principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285. Lilly sells pemetrexed in the United States under the trademark ALIMTA® for treatment of patients with malignant pleural mesothelioma, or for the initial treatment of locally advanced or metastatic nonsquamous non-small cell lung cancer, and other forms of lung cancer. ALIMTA® is covered under U.S. Patent No. 5,344,932, which is owned by The Trustees of Princeton University and licensed exclusively to Lilly.

Dr. Reddy's Ltd. is a drug manufacturer with a principal executive office at Hyderabad, Telangana 500 034, India, and Dr. Reddy's Inc. is a corporation organized and existing under the laws of the State of

New Jersey. Dr. Reddy's is in the business of manufacturing, marketing, and selling both generic and non-generic drug products. In December 2015, Dr. Reddy's notified Lilly that it had submitted to the FDA New Drug Application No. 208297, a product that will be marketed as competing products to ALIMTA®

Dr. Clet Niyikiza ("Dr. Niyikiza"), the inventor of the '209 Patent, is a mathematician that was employed by Lilly in the 1990s to help with the clinical development of cancer compounds. In early 1997, Dr. Niyikiza performed a series of statistical analyses, known as multivariate analyses, on more than 60 variables in patients participating in pemetrexed clinical trials in efforts to better understand which patients were likely to develop the sporadic toxicities observed with pemetrexed. The problem the invention solves is toxicity in patients receiving chemotherapeutic treatment with pemetrexed. In particular, the '209 Patent provides for a method that mitigates the toxicity associated with pemetrexed treatment, using the vitamin pretreatment regimen of vitamin B12 and folic acid. (Filing No. 231 at 35.)

The primary focus of this infringement trial is on whether Dr. Reddy's label, specifically the use of pemetrexed ditromethamine product described therein, infringes the '209 Patent, which uses pemetrexed disodium, under the doctrine of equivalents. The '209 Patent covers the method of administration of ALIMTA®, requiring that physicians co-administer the drug with folic acid and vitamin B12 to reduce the incidence of patient toxicity caused by ALIMTA®. Claim 12 of the '209 Patent describes an improved method for administering

pemetrexed disodium, comprising "a) administration of between 3500 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 B12, prior to the first administration of pemetrexed disodium; and c) administration of pemetrexed disodium." (Filing No. 1-1 at 9).

The parties disagree on the relevance of any chemical differences between pemetrexed disodium and pemetrexed ditromethamine, nevertheless both Lilly's and Dr. Reddy's experts, Dr. Bruce A. Chabner, M.D., ("Dr. Chabner"), Rodolfo Pinal ("Dr. Pinal"), and George Gokel ("Dr. Gokel"), agreed on what the differences were between the two chemical compounds. Sodium is an inorganic metallic salt, and tromethamine is an organic, nonmetallic salt. (Filing No. 231 at 181.) Tromethamine weighs more than sodium. *Id.* Because tromethamine can raise pH, it can be used as buffer; however, sodium may not be used as a buffer because it cannot be used as a pH adjuster. *Id.* at 158. Additionally, it is undisputed that pemetrexed disodium is more hygroscopic and absorbs more than twice the amount of water than pemetrexed ditromethamine. *Id.* at 173. As noted in the Court's claim construction finding, regardless if pemetrexed disodium or pemetrexed ditromethamine is administered to the patient, the patient receives an intravenous solution of pemetrexed in treating the patient's cancer. The evidence presented at trial demonstrates that the person who solves the problems to which the claims are addressed requires a medical oncologist.

II. Conclusions of Law

A. Prosecution History Estoppel

In the Court's amended Final Pretrial Entry, the Court permitted the parties, at trial, to supplement the summary judgment record on the issue of prosecution history estoppel. (Filing No. 216 at 4.) In its Entry on Motion for Summary Judgment of Noninfringement, the Court found Lilly was not barred, as a matter of law under prosecution history estoppel, from asserting the doctrine of equivalents. (Filing No. 199 at 15.) ("Lilly has met its burden of showing that it did not surrender the equivalent in question because the choice of pemetrexed salt is tangential to the reasons for the amendment and summary judgment is precluded on this issue.")

As in the summary judgment briefing, Dr. Reddy's continues to collapse the foreseeability exception with the tangential exception, on which the Court relied in holding in Lilly's favor. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 733 (2002). Dr. Reddy's focuses on the unexplained reason that Lilly limited the '209 Patent to pemetrexed disodium, in essentially arguing that Lilly could have drafted a better claim. ("[A]" patentee cannot argue in litigation that a narrowing amendment in prosecution was excessive, and that the patentee could have avoided the prior art (and gained allowance) with a less severe amendment that would have literally embraced the accused equivalent." (Filing No. 234 at 6).) In any event, Lilly has explained the reason for the narrowing amendment: it was narrowed to overcome a rejection in view of Arsenyan, a prior art article about a different antifolate, methotrexate. (Filing

No. 235 at 35.) The Court agrees with Lilly that at trial Dr. Reddy's expert, Dr. Gokel, did nothing to dispute or add to the summary judgment record as to the prosecution history evidence from which tangentiality is analyzed. (Filing No. 232 at 42.) Accordingly, the Court again concludes that Lilly's rationale for limiting its claim to pemetrexed disodium (to avoid a rejection based on the prior art Arsenyan) is tangential to the accused equivalent—pemetrexed ditromethamine. The Court directs the parties to Filing No. 199 for a more detailed analysis regarding the Court's holding that Lilly has rebutted the presumption that prosecution history estoppel applies.

B. Disclosure-Dedication Rule

Another issue, extensively briefed by the parties on summary judgment, was the disclosure-dedication doctrine. Again, the trial record and the summary judgment record contain significant overlap as to this issue. Because Lilly did not move for summary judgment on this issue, it was not decided on summary judgment, rather it was fleshed out by expert testimony at the trial. The disclosure-dedication rule bars a doctrine of equivalents claim when a patentee discloses but does not claim subject matter. *Johnson & Johnston Associates, Inc. v. R.E. Service Co., Inc.*, 285 F.3d 1046, 1054 (Fed. Cir. 2002).

As noted in the Court's Entry on Motion for Summary Judgment of Noninfringement, it is undisputed that the '209 Patent's specification did not expressly disclose pemetrexed ditromethamine. Rather, Dr. Reddy's bases its disclosure-dedication argument on the fact that the '209 Patent referenced

U.S. Patent No. 4,997,838 to Akimoto and that from Akimoto the hypothetical person of skill in the art ("POSA") could find pemetrexed ditromethamine disclosed among the alternatives disclosed in Akimoto. (Filing No. 234 at 25-26.) 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). Although the '209 Patent did not expressly incorporate Akimoto by reference, it cited that preferred examples of antifolates can be found in the derivatives described by Akimoto. (Filing No. 1-1 at 5.) Because this issue hinged on what a POSA would recognize as unclaimed subject matter disclosed in the '209 Patent specification and if Akimoto's disclosures in combination would disclose pemetrexed ditromethamine, it left a factual dispute for trial.

At trial, Dr. Pinal testified that Akimoto included pemetrexed and any "pharmaceutically acceptable

salt thereof." (Filing No. 231 at 249.) From this concession, Dr. Reddy's argues that pharmaceutically accepted salts would include substituted ammonium salts of which tromethamine is one of a few FDA-approved substituted ammonium salts. (Filing No. 234 at 24.) Thus, Dr. Reddy's contends that a POSA would have recognized pemetrexed in combination with tromethamine as an alternative to pemetrexed disodium. (Filing No. 234 at 26-27.) Lilly responds that while Dr. Pinal testified that pemetrexed is within the genus covered by Akimoto, Dr. Pinal also testified that Akimoto disclosed a genus of thousands of antifolates. (Filing No. 231 at 227.) Further, tromethamine is not specifically disclosed in any referenced patent nor is the compound pemetrexed ditromethamine. (Filing No. 238 at 16-17.) Because Akimoto was not expressly incorporated, as required, in the '209 Patent, and in any event Akimoto does not specifically disclose pemetrexed ditromethamine as an alternative to pemetrexed disodium, the disclosure-dedication rule does not bar Lilly's doctrine of equivalents claim. At most, the reference to Akimoto and what was contained therein amounts to a generic reference which does not dedicate all members of a particular genus to the public.

C. Doctrine of Equivalents

Lilly asserts, and the Court agrees, that healthcare providers using the proposed Dr. Reddy's product will directly infringe under the doctrine of equivalents, and that Dr. Reddy's is liable as an indirect infringer under 35 U.S.C. §§ 271(b) and (c).

As an initial matter, the relevant POSA must be defined for a doctrine of equivalents analysis. "What constitutes equivalency must be determined against the context of the patent, the prior art, and the particular circumstances of the case." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.,* 520 U.S. 17, 24 (1997) (citation omitted). Thus, a POSA becomes an important factor as to "whether persons reasonably skilled in the art would have known of the interchangeability of an ingredient not contained in the patent with one that was." *Id.* Dr. Reddy's contends that the POSA should be the type of person who solves the problems to which the claims are addressed such as Dr. Niyikiza, the inventor of the patent.[1] (Filing No. 234 at 28, 30.) ("The POSA could be trained as a chemist, biochemist, pharmaceutical scientist, physician, or molecular biologist. The POSA, even if he is a physician, should have a strong background in chemistry and biochemistry, understand the folate pathways and metabolism, and have a solid grasp of acid-base.") Dr. Reddy's proposed POSA would examine the doctrine of equivalents from the perspective of the chemical and biochemical properties between pemetrexed disodium and pemetrexed ditromethamine. (Filing No. 234 at 30.) Lilly responds that the '209 Patent makes clear, from the plain language of the claims and testimony from the inventor, Dr. Niyikiza, that the POSA is directed to a medical oncologist. (Filing No. 235 at 13.) Lilly's proposed POSA would perform a doctrine of

[1] Dr. Niyikiza is a statistician, with a Ph.D. in mathematics and statistics, not a chemist, biochemist, pharmaceutical scientist, physician, or molecular biologist. (Filing No. 238 at 21.)

equivalents analysis focusing on the medical treatment aspects of the claims. (Filing No. 238 at 19.) This Court has "previously defined the POSA as 'a medical doctor who specializes in oncology or a medical doctor with extensive experience in the areas of nutritional sciences involving vitamin deficiencies [,who] collaborated with medical oncologists who have knowledge and experience in the treatment of cancer through the use of antifolates.'" *Eli Lilly and Company v. Teva Parenteral Meds., Inc.,* 1:10-cv-1376-TWP-MPB, 2012 WL 2358102, at *4 (S.D. Ind. June 20, 2012), ECF 115 at 8. Essentially, the point of contention between the proposed POSAs advanced by the parties is whether the POSA is a chemist or an oncologist.

Dr. Reddy's POSA definition is defeated by the plain language of the '209 Patent as the invention explicitly identifies it as "a method of reducing the toxicity associated with the administration of an antifolate to a mammal …" (Filing No. 1-1 at 5). Lilly is correct that the relevant POSA who works to mitigate the toxicities of chemotherapy would be an oncologist, particularly an oncologist with extensive experience in the areas of nutritional sciences involving vitamin deficiencies as confirmed by Dr. Chabner. Thus, equivalency is examined from an oncologist POSA. The relevant POSA is critical (and dispositive) to resolving the doctrine of equivalents analysis in the context of the claims as to whether the POSA would focus on the different salt forms of pemetrexed disodium and pemetrexed ditromethamine as being substantial differences, or instead would focus on the pemetrexed treatment that the patient receives.

The United States Supreme Court has set out two frameworks for evaluating equivalence—the function, way, result test (whether the accused product performs 'substantially the same function in substantially the same way to obtain the same result'), and the insubstantial differences test (whether the accused product or process is substantially different from what is patented). *Mylan Institutional LLC v. Aurobindo Pharma Ltd.,* 857 F.3d 858, 866-67 (Fed. Cir. 2017) ("Thus, the Court seemingly blessed two equivalents tests, leaving to the lower courts in future cases the choice of which to apply.") (quoting *Graver Tank & Mfg. Co. v. Linde Air Prod. Co.,* 339 U.S. 605, 608 (1950). Additionally, the Federal Circuit, relying on *Graver*, noted that the insubstantial differences test may be more appropriate in chemical arts cases. *Id.* ("The Supreme Court was surely correct in stating that non-mechanical cases may not be well-suited to consideration under the FWR test.") Because equivalence in this case is based on chemical properties, the Court determines that the insubstantial differences test is the more appropriate framework for evaluating equivalence.

"Under the doctrine of equivalents, a claim limitation not literally met may be satisfied by an element of the accused product if the differences between the two are 'insubstantial' to one of ordinary skill in the art." *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.,* 320 F.3d 1339, 1351 (Fed. Cir. 2003). "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). As noted previously, the relevant POSA, in this case, is a medical oncologist. Dr. Chabner testified that the invention claimed in the '209 Patent relates to "using pretreatment B12 and folic acid to mitigate the toxicity of pemetrexed when it's given to a patient with cancer." (Filing No. 231 at 70.) Additionally, Dr. Chabner testified that the pemetrexed disodium could not exert an anti-cancer effect in solid form, thus the POSA would understand that pemetrexed disodium is administered by first putting it into solution and then intravenously administering the solution to the patient for an anti-cancer effect. *Id.* at 72.

Under the relevant context that the claim relates to medical treatment, pemetrexed ditromethamine treats the patient's cancer in exactly the same way as pemetrexed disodium. It is undisputed that when both pemetrexed disodium and pemetrexed ditromethamine are placed in solution, that both compounds dissociate completely in solution resulting in free pemetrexed and therapeutically irrelevant counterions. *Id.* at 208-09. In fact, in aqueous solution, the two products will be identical. (Filing No. 231 at 212.) Recognizing these similarities, Dr. Reddy's relied on Lilly's clinical trials of pemetrexed disodium, in demonstrating the safety and efficacy of its product, when it told the FDA that the salt form does not matter when it comes to treating the patient to support approval of its NDA product. (Filing No. 231 at 80-81.) It is undisputed that the products are bioequivalent; however, the parties disagree on whether there is patent equivalence in the context of the claimed method. (Filing No. 234 at 42-43; Filing No. 238 at 24.) "[W]hen a commercial product meets

all of the claim limitations, then a comparison to that product may support a finding of infringement." *Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1289 (Fed. Cir. 2010).

The differences in the chemical properties between pemetrexed disodium and pemetrexed ditromethamine with regards to solubility, stability, pH, and buffering capacity are irrelevant in the context of the claimed method including this Court's claim construction. (Filing No. 234 at 42.) Additionally, the theoretical phenomenon of the difference of salting out between the two products is irrelevant, as ALIMTA®'s label "requires the solution to be clear prior to administration and specifically instructs physicians not to administer it if any particulate matter is observed." (Filing No. 235 at 22-23.) To be sure, the evidence shows that tromethamine differs from sodium with regards to the chemical properties as alleged by Dr. Reddy's. Lilly does not dispute that there are differences when the products are in solid form, instead Lilly argues that the differences are insubstantial. (Filing No. 231 at 80.) The Court agrees. The differences are irrelevant in the context of the claimed method which is a liquid administration of pemetrexed sodium. What is in fact ultimately administered to the patient is injectable pemetrexed ions that enter the patient's cells. (Filing No. 231 at 79-80.) The products are identical in liquid form as pemetrexed is the active moiety in both Dr. Reddy's and Lilly's products dissolved in solution. (*See* Filing No. 232 at 124-25; Filing No. 235 at 18.) Furthermore, Dr. Reddy's incorrectly relies on a chemist POSA in posing nonequivalence, who would not administer the drugs to a patient as the '209

Patent is a claimed method of treatment. Accordingly, Lilly has shown by a preponderance of the evidence that Dr. Reddy's product is equivalent to Lilly's product.

D. Inducement and Contribution to Infringement of '209 Patent

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). 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). Because Dr. Reddy's does not provide care to patients, the direct infringement is attributed to the healthcare providers.

"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). 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).

Relying on *Commil USA, LLC v. Cisco Sys., Inc.,* 135 S. Ct. 1920, 1928 (2015), Dr. Reddy's contends that Lilly cannot prove Dr. Reddy's specifically intended to infringe because specific intent requires proof that Dr. Reddy's knew the acts were infringing. (Filing No. 234 at 44.) As evidence that Dr. Reddy's did

not know its product would infringe the '209 Patent, Dr. Reddy's offers that it selected tromethamine, in good-faith belief, to avoid infringing the '209 Patent. *Id.* at 45. As Lilly correctly points out, Dr. Reddy's ignores how specific intent can be shown in the Hatch-Waxman context, particularly how specific intent can be inferred from an accused product's labeling. *AstraZeneca LP v. Apotex, Inc.* considered similar facts where Apotex's product development team testified that it "never intended to instruct or encourage either physicians or patients to use its generic drug once-daily." *Id*. However, AstraZeneca held "[t]he pertinent question is whether the proposed label instructs users to perform the patented method. If so, the proposed label may provide evidence of Apotex's affirmative intent to induce infringement." *Id.* at 1060. Specific intent and liability for inducement are established if "the product labeling that Defendants seek would inevitably lead some physicians to infringe." *Eli Lilly and Company v. Teva Parenteral Meds., Inc.,* 845 F.3d 1357, 1368-69 (Fed. Cir. 2017); *Takeda Pharms. USA, Inc. v. West-Ward Pharm. Corp., 758 F.3d 625, 631 (Fed. Cir. 2015).* Dr. Reddy's has provided no defense to the infringing pretreatment regimen portion of its label that this Court has already found induced infringement in another case with label instructions substantively identical to those in Dr. Reddy's Label. *Eli Lilly and Company v. Teva Parenteral Meds., Inc.,* No.1:10-cv-1376-TWP-MPB, 126 F.Supp.3d 1037 (S.D. Ind. Aug. 25, 2015).

As noted previously, administration of pemetrexed ditromethamine according to Dr. Reddy's label infringes Lilly's product under the doctrine of equivalents. 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."). "We have long held that the sale of a product specifically labeled for use in a patented method constitutes inducement to infringe that patent, and usually is also contributory infringement." *Eli Lilly & Co. v. Actavis Elizabeth LLC,* 435 F. App'x 917, 926 (Fed. Cir. 2011) (citing *AstraZeneca LP v. Apotex, Inc.,* 633 F.3d 1042, 1060 (Fed.Cir.2010)).

This Court has determined that Dr. Reddy's product infringes the '209 Patent under the doctrine of equivalents. Accordingly, it cannot avoid intent or infringement on the bases that it possessed a "good faith belief that its proposed product[s] would not infringe." Moreover, the Court finds, based on a preponderance of the evidence, Dr. Reddy's label instructs users to perform the patented method by both inducing and contributing to infringement and that Dr. Reddy's had the requisite specific intent and knowledge that its label would cause such infringement. Dr. Reddy's product does not have a substantial noninfringing use to avoid contributory infringement. A physician administering Dr. Reddy's product would constitute direct infringement under § 271(a); thus, the use the Dr. Reddy's NDA products would constitute inducement and contributory

infringement of the '209 Patent by Dr. Reddy's under 35 U.S.C. § 271(b), (c).

III. Conclusion

Based upon the foregoing findings of fact and conclusions of law, the Court concludes that Lilly has shown by a preponderance of the evidence that the asserted claims of the '209 Patent would be infringed by Dr. Reddy's product under the doctrine of equivalents based upon inducement and contributory infringement. The Court finds that Dr. Reddy's product indirectly infringes the asserted claims of the '209 Patent, and finds in favor of Eli Lilly And Company and against Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd.. Final judgment shall issue separate from this Entry.

SO ORDERED.

Date: 6/22/2018

[handwritten: signature]
TANYA WALTON PRATT, JUDGE
United States District Court
Southern District of Indiana

Appendix D

UNITED STATES DISTRICT COURT FOR THE SOUTHERN DISTRICT OF INDIANA

No. 1:16-cv-00308-TWP-MPB

ELI LILLY AND COMPANY,

Plaintiff,

v.

DR. REDDY'S LABORATORIES, LTD. and DR. REDDY'S LABORATORIES, INC.,

Defendants.

Dated: June 22, 2018

ENTRY ON MOTION FOR SUMMARY JUDGMENT OF NONINFRINGEMENT

This matter is before the Court on Defendants Dr. Reddy's Laboratories, LTD.'s and Dr. Reddy's Laboratories, Inc.'s (collectively, "Dr. Reddy's") Motion for Summary Judgment of Noninfringement of the U.S. Patent 7,772,209 (the "'209 Patent") (Filing No. 132). Plaintiff Eli Lilly and Company ("Lilly") initiated this Hatch-Waxman litigation alleging that Dr. Reddy's New Drug Application No. 208297 and the use of the product described therein, infringe Lilly's '209 Patent. On November 9, 2017, oral argument was held on the Motion at which the parties made helpful presentations. For the reasons stated below, the Court

determines that summary judgment is not appropriate and Dr. Reddy's Motion is denied.

I. BACKGROUND

The '209 Patent describes a method of administering a chemotherapy drug, pemetrexed disodium, with a pretreatment regimen of vitamin B12 and folic acid ("pretreatment regimen"), which is marketed by Lilly under the trade name ALIMTA®. The '209 Patent has been the subject of two 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]. 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 B12 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.*

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.[2] To avoid rejection of its patent in view of Arsenyan, Lilly narrowed the

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

[2] Both methotrexate and pemetrexed fall within the broader antifolate group, but they target different enzymes. (Filing No. 146 at 44.)

scope of its claims from a broad category of antifolates to specifically pemetrexed disodium. (Filing No. 133-1 at 124; Filing No. 146 at 30.)

Dr. Reddy's is a drug manufacturer and does not treat patients, therefore any infringement would be based on indirect infringement. Dr. Reddy's set out to avoid infringing the '209 Patent by designing a different product. It ran experiments to investigate different salts, and chose tromethamine. Unlike the generic drug manufacturers that used pemetrexed disodium in the proposed generic drugs in previous trials, Dr. Reddy's seeks to market a new product that uses pemetrexed ditromethamine, rather than pemetrexed disodium.

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." Tromethamine is an inorganic, metallic salt, whereas sodium is an organic, nonmetallic salt. (Filing No. 135 at 8.) 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. The products are sold in solid form. At issue is claim 12 of the '209 Patent. 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 B12, prior to the first administration of pemetrexed disodium; and
>
> c) administration of pemetrexed disodium.

(Filing No. 1-1 at 9).

As previously noted, Dr. Reddy's product uses a different pemetrexed compound: pemetrexed ditromethamine. In addition, Dr. Reddy's label on the administration of the pemetrexed ditromethamine differs from Lilly's in that Dr. Reddy's label instructs that pemetrexed ditromethamine should be reconstituted and diluted with 5% dextrose in water ("dextrose"), whereas Lilly's label instructs that the pemetrexed disodium should be reconstituted and diluted in saline solution. (Filing No. 92-3; Filing No. 179-1.) Dr. Reddy's label states "[c]oadminstration of pemetrexed with other drugs and diluents has not been studied, and therefore is not recommended." (Filing No. 92-3 at 9.) Dr. Reddy's label also instructs that the pretreatment regimen be followed and mitigates the severe toxicities that pemetrexed can otherwise cause. *Id.* at 42.

Both Dr. Reddy's and Lilly's labels indicate that its products are to be administered along with cisplatin for some patients. *Id.* at 11. Before cisplatin can be administered to a patient it requires and is standard practice to prehydrate it with saline to prevent serious kidney toxicity. (Filing No. 146 at 13-14.) Dr. Reddy's label instructs that the cisplatin be administered intravenously approximately thirty

minutes after the end of administration of pemetrexed treatment. (Filing No. 92-3 at 37.) Saline is commonly used in intravenous administration for many different drugs.

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 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).

III. Discussion

As an initial matter, the Court notes that Lilly recently changed its ALIMTA® label in response to the Food and Drug Administration's ("FDA") instructions to change various aspects of the label. Nevertheless, both parties agree that the new label does not change the substance or legal theories of any of the briefings previously submitted to the Court and that the parties are prepared to go forward with the proceedings as they currently stand. (Filing No. 182 at 7-10.)

Lilly argues that Dr. Reddy's product infringes under two theories: literal infringement and the doctrine of equivalents. (Filing No. 146 at 19.) The Court will first address the embedded claim construction issue and then address each infringement theory.

A. Claim Construction

The claims define the scope of patent protection. *Johnson & Johnston Associates, Inc. v. R.E. Service Co., Inc.,* 285 F.3d 1046, 1052 (Fed. Cir. 2002). The words of a claim are generally given their ordinary and customary meaning, as understood by a person of skill in the art ("POSA") when the patent was filed. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005)

(*en banc)*. When the ordinary meaning of a claim is disputed, the Federal Circuit has directed courts to look to the patent specification, which is the single best guide to the meaning of a disputed term. *Id.* at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). "The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Phillips,* 415 F.3d at 1316. Courts may also consider extrinsic evidence, such as expert testimony or dictionaries, but such evidence is "less significant" than the patent specification and prosecution history (*i.e.,* the written history of patentee's prior dealings with the patent office). *Id.* at 1317. "Importantly, the 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.* "[I]t is necessary to consider the specification as a whole, and to read all portions of the written description, if possible, in a manner that renders the patent internally consistent." *Budde v. Harley-Davidson, Inc.*, 250 F.3d 1369, 1379-80 (Fed. Cir. 2001). "A claim construction that excludes a preferred embodiment … is rarely, if ever correct." *SanDisk Corp. v. Memorex Products, Inc.*, 415 F. 3d 1278, 1285 (Fed. Cir. 2005) (citation and internal quotation omitted).

At the hearing, the parties set forth different constructions of claim 12's meaning. (*See* Filing No. 182 at 23, 30.) It is undisputed that claim 12 is a method claim, but the parties essentially dispute the meaning of "administration of pemetrexed disodium."

Lilly argues that "administration of pemetrexed disodium" refers to the act of giving the patient the liquid solution of pemetrexed disodium after it has been diluted and reconstituted because no salt form is given to patients. (Filing No. 182 at 30.) Lilly explains that its experts have opined that a POSA would understand claim 12 to embrace the meaning of a solution with pemetrexed ions and two sodium ions that is given to patients intravenously. *Id.* Dr. Reddy's argues that this construction would improperly require "changing each instance of 'pemetrexed disodium' in the claims to a 'solution comprising pemetrexed ions and sodium ions.'" (Filing No. 167 at 3.)

"Claim construction begins with the language of the asserted claims." *SanDisk*, 415 F.3d at 1284 (citation omitted). As stated previously the relevant asserted claim at issue is "administration of pemetrexed disodium". The dispute between the parties' different claim construction arguments turns on the word "administration". This is primarily due to the fact that the patient receives the product through a liquid solution, but ALIMTA® is sold in solid or salt form.[3]

The Federal Circuit prefers intrinsic evidence over extrinsic evidence in construing claims. *See Phillips*, 415 F.3d at 1317 ("However, while extrinsic evidence 'can shed useful light on the relevant art,' we have explained that it is 'less significant than the intrinsic record in determining 'the legally operative

[3] Although Dr. Reddy's product is not on the market yet, it is also being proposed to sell in a solid form.

meaning of claim language.'") (citations omitted). Turning to the intrinsic evidence first, the Court begins with the specification. The specification must conclude with the claims "particularly pointing out and distinctly claiming the subject matter" which the applicant regards as his invention. *See* 35 U.S.C. § 112. This apprises the public of the metes and bounds of the subject matter for which the inventor seeks patent protection.

The '209 Patent's specification distinctly claims pemetrexed disodium. The prosecution history is consistent with this result. "The court must always consult the prosecution history, when offered in evidence, to determine if the inventor surrendered disputed claim coverage." *SanDisk*, 415 F.3d at 1286. Here, the prosecution history reveals that the amendments to the detailed description section of the specification as well as the claims were made in response to the U.S. Patent and Trademark Office's ("Patent Office") rejections. (Filing No. 133-1 at 147-48.) Lilly limited the chemical compound used in claim 12 to pemetrexed disodium. "As a basic principle of claim interpretation, prosecution disclaimer promotes the public notice function of the intrinsic evidence and protects the public's reliance on definitive statements made during prosecution. *SanDisk*, 415 F.3d at 1287 (citation omitted).

Unlike pemetrexed disodium, the parties' dispute over the word "administration" is not completely resolved by resorting to intrinsic evidence alone. The specification, claims, nor prosecution history do not resolve this dispute. "There is no 'clear and unmistakable' disclaimer if a prosecution argument is

subject to more than one reasonable interpretation, one of which is consistent with a proffered meaning of the disputed term." *Id.* (citation omitted). The '209 Patent does reveal that it is a method invention, but the claims do not address how ALIMTA® *i.e.,* pemetrexed disodium, is actually given to the patient. That requires reading the label's detailed directions. Both products' labels require the powdered form of the drugs to be diluted and reconstituted, using different liquid solvents.[4] The expert reports shed light on what a POSA would understand "administration" to mean. The Court finds it very persuasive that both products are administered in liquid form to be indicative that a POSA would understand the '209 Patent to refer to a method of liquid administration of pemetrexed disodium.

What happens to pemetrexed disodium or pemetrexed ditromethamine after the liquid solution is prepared and administered to the patient is not a question that needs to be resolved in construing claim 12. In any event, the parties agree on the science of what happens during the administration of the liquid solution the patient. "And Dr. Chabner is saying, well, I think people would understand the claim to mean this. And, basically, what he's saying is, because that makes sense, that's what Lilly should have done, *people know that it's the pemetrexed that matters*." (Filing No. 182 at 51) (emphasis added). The patient receives pemetrexed treatment. "Claim construction is a matter of resolution of disputed meanings and technical scope, to clarify and when necessary to

[4] Lilly's label requires saline, while Dr. Reddy's label requires dextrose.

explain what the patentee covered by the claims, for use in the determination of infringement. It is not an obligatory exercise in redundancy." *U.S. Surgical Corp., v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997). Having already determined based on the intrinsic evidence, Lilly claimed "pemetrexed disodium," the Court declines further claim construction based on Lilly's assertion that the term "embraces the administration in liquid form of pemetrexed ions in combination with two sodium ions. (Filing No. 182 at 30.) In sum, the Court construes claim 12's "administration of pemetrexed disodium" language to refer to a liquid administration of pemetrexed disodium. The liquid administration is accomplished by dissolving the solid compound pemetrexed disodium into solution as instructed by the ALIMTA® label. This construction is consistent with the '209 Patent's specification and the plain meaning of claim 12 as well as the prosecution history. It is undisputed that a POSA would understand that the '209 Patent refers to a method of liquid administration because pemetrexed is the active ingredient that treats the cancer and the patient receives the solution intravenously. Further, this construction adheres to the bedrock patent claim construction principle to not exclude a preferred embodiment *i.e.*, pemetrexed disodium, and renders the patent internally consistent.

B. 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's theory of literal infringement involves Dr. Reddy's product's use in combination with certain patients that require another chemotherapy drug called cisplatin. In these instances, Dr. Reddy's label instructs that the pemetrexed product is to be infused thirty minutes before cisplatin. Cisplatin requires prehydration with saline solution—sodium chloride. (Filing No. 146 at 2.) Lilly contends that the cisplatin use and pemetrexed infusion will overlap because they are administered thirty minutes apart and that when this happens Dr. Reddy's product will mix with the saline solution due to the prehydration requirement. The resulting solution will contain pemetrexed molecules and sodium and tromethamine ions that disassociate from each other. Lilly explains that Dr. Reddy's product will be mixed with saline solution as it is being infused into a patient through the same intravenous line as the saline prehydration. The resulting solution will contain pemetrexed and sodium ions—that is pemetrexed disodium.

Dr. Reddy's responds that Lilly's theory of literal infringement would require healthcare providers to completely disregard its label instructions to use the Dr. Reddy's product with dextrose solution only. Lilly relies on the fact that the label does not explicitly instruct not to use saline and that a POSA would know that saline is suitable for use with pemetrexed drugs as Lilly's product has been safely administered with saline for over a decade. (Filing No. 146 at 15.) Dr. Reddy's label states that co-administration of Dr. Reddy's products with other diluents has not been studied and is therefore not recommended. Dr. Reddy's argues that Lilly's literal infringement claim

must prove that the Dr. Reddy's label instructs users to mix the Dr. Reddy's product with saline. Dr. Reddy's label also states that its product should not mix with anything except dextrose before it is infused. Dr. Reddy's also explains that even if healthcare providers mixed Dr. Reddy's pemetrexed ditromethamine with saline this would not be "administration of pemetrexed disodium" as required by Lilly's patent claims.

The claim construction issue has been resolved as a liquid administration of pemetrexed disodium. For purposes of summary judgment, the Court must credit Lilly's literal infringement theory that cisplatin's requirement and established practice of saline prehydration would overlap with the pemetrexed infusion and the two would mix via healthcare providers administering both through the same intravenous line. Furthermore, because saline contains sodium ions that this would result in infringement when Dr. Reddy's pemetrexed ditromethamine product is mixed with the saline resulting in a liquid administration of the pemetrexed disodium solution. Based on the foregoing, viewing the facts in a light favorable to Lilly, there are disputed issues of material fact as to whether every limitation of the asserted claim is literally met by the allegedly infringing device. Thus, Dr. Reddy's Motion for Summary Judgment of Noninfringement (Filing No. 132) is denied as to literal infringement.

C. Doctrine of Equivalents

"The doctrine of equivalents extends the right to exclude beyond the literal scope of the claims." *Johnson*, 285 F.3d at 1053. "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. Dr. Reddy's argues that Lilly's doctrine of equivalents infringement claim is foreclosed by prosecution history estoppel, the disclosure dedication rule, and doctrine of vitiation. The Court will address each of these threshold arguments in turn.

1. Prosecution History Estoppel

Dr. Reddy's argues that prosecution history estoppel bars Lilly's doctrine of equivalents claim at the threshold as a matter of law. (Filing No. 182 at 12.) 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 Dr. Reddy'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. Lilly argues that the tangential exception applies here, in that the different salt forms of pemetrexed used bear no more than a tangential relationship to the rationale for the underlying amendment. (Filing No. 146 at 23.) Lilly concedes that the amendment was to overcome a rejection in view of Arsenyan, however it explains that Arsenyan is a prior art article about the administration of a compound called methotrexate, also an antifolate but distinguishable from pemetrexed.

Dr. Reddy's incorrectly reads *Festo* to hold that the rationale for the amendment must be both unforeseeable and tangential, but explains that even if tangential is an independent basis, Lilly is nevertheless precluded from asserting doctrine of equivalents because Lilly's narrowing amendment went to the identity of a particular type of antifolate—pemetrexed disodium. (Filing No. 167 at 6.) Dr. Reddy's goes on to cite Lilly's prosecution of the European equivalent of the '209 Patent where Lilly claimed pemetrexed broadly and used a dependent claim to claim the salt form: pemetrexed disodium. (Filing No. 182 at 16U.) This argument goes to foreseeability that Lilly allegedly knew how to draft a broad pemetrexed claim that was not narrowly limited to disodium salt.

Lilly argues that for the tangential exception "it makes no difference whether Lilly 'limited the scope of drugs in the claimed method' in a way that turned out to exclude the accused pemetrexed ditromethamine." Because pemetrexed, the active drug substance, actually treats the cancer patient, and pemetrexed disodium and pemetrexed ditromethamine are very similar, this exception necessarily presents a battle of the experts issue. In fact, it is undisputed that a POSA would understand that pemetrexed is the active antifolate (or drug) in both products.

In *Regents of University of Cal. v. Dakocytomation Cal. Inc.*, 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 district court granted summary judgment of noninfringement to the maker of the accused products because it held that the patentees had narrowed the scope of "blocking nucleic acid" during prosecution which barred the patentees from asserting the peptide nucleic acid equivalent. *Id.* The Federal Circuit reversed holding "[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.

The present case is similar to the distinction presented in *Regents*. The '209 Patent's specification describes a method for pemetrexed disodium treatment. Lilly's expert opined that a POSA would understand pemetrexed is the active antifolate that inhibits the enzymes at issue and treats the cancer. Dr. Reddy's argues that the salt form used in the patent goes to the identity of the antifolate that Lilly sought to claim and is thus barred from claiming pemetrexed as a class under prosecution history estoppel.

The prosecution history reveals that the Patent Office rejected various Lilly claims due to the prior art Arsenyan.

> Claims 2, 7, 10, 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Arsenyan et al. (Abstract; *Onkol.*, *Nauchn.*, (1978) 12(10); 49-54. Arsenyan et al. teaches a method of pretreating mammals (mice) with various types of cancer with methylcobalamin (a vitamin B12 derivative which reduces methylmalonic acid) then administering methotrexate (an antifolate), and reports increased tumor inhibition and survival with methylcobalamin treatment.

(Filing No. 133-1 at 115.) The Arsenyan prior art rejection also served as the basis for an obviousness rejection. (Filing No. 133-1 at 117.) The prior art rejections thus went to patentability. The Patent Office's communications do not refer to pemetrexed broadly, but also refer to pemetrexed disodium in

combination with the pretreatment regimen as not being anticipated by the prior art. This is probably because ALIMTA® is sometimes used interchangeably with pemetrexed disodium during Lilly's patent prosecution. (*See* Filing No. 133-1 at 136.) At one point the Patent Office rejected Lilly's use of the trade name ALIMTA® in its claims as being vague and indefinite language, and Lilly responded with substituting pemetrexed disodium for ALIMTA®. (Filing No. 133-1 at 115.)

To overcome the prior art rejection, Lilly argued that the invention was new and nonobvious because it used the pretreatment regimen in combination with administration of pemetrexed disodium to treat the cancer and reduce the toxicities associated with pemetrexed disodium administration. (Filing No. 133-1 at 127.) The narrowing amendment (from antifolates as a class to pemetrexed disodium) was only tangential to the accused pemetrexed equivalent—pemetrexed ditromethamine. Thus, Lilly has met its burden of showing that it did not surrender the equivalent in question because the choice of pemetrexed salt is tangential to the reasons for the amendment and summary judgment is precluded on this issue.

2. Disclosure Dedication Doctrine

Dr. Reddy's argues that Lilly's equivalents claim is also barred by the disclosure dedication rule. "[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,* 429 F. 3d 1379.

It is undisputed that the '209 Patent's specifications do not expressly disclose pemetrexed ditromethamine. Dr. Reddy's bases its disclosure dedication argument on the fact that the '209 Patent referenced another patent, Akimoto, and the pemetrexed salt derivatives described by Akimoto would include pemetrexed ditromethamine. (Filing No. 167 at 13.) Lilly responds that "[t]he Federal Circuit has recognized the possibility of using the specification of a different patent only where it was expressly incorporated by reference." (Filing No. 146 at 28.)

The disclosure dedication rule has limitations. 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). There are two issues with Dr. Reddy's disclosure dedication argument. First, the '209 Patent did not expressly incorporate Akimoto by reference. Rather, the '209 Patent cites that preferred examples of antifolates can be found in the derivatives described by Akimoto. (Filing No. 1-1 at 5.) Dr. Reddy's argues that if a POSA went looking in Akimoto that the POSA would find pemetrexed and other substituted ammonium salts. To this second issue, Lilly responds that its experts will testify that Akimoto discloses a broader genus which would balloon out to over 200,000 compounds. The Court agrees that because of this large generic genus, no POSA would understand Akimoto to specifically disclose pemetrexed, tromethamine, or pemetrexed ditromethamine from the broader genus of compounds that Akimoto discloses unless they knew to go looking for it. The disclosure dedication issue presented in this case hinges on what a POSA would recognize as unclaimed subject matter disclosed in the '209 Patent specification and if Akimoto's disclosures in combination would disclose pemetrexed ditromethamine. The Akimoto reference does not satisfy the disclosure dedication rule's requirements of a specific identification that amounted to a disclosure of an alternative to a claim limitation. 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.

3. Doctrine of Vitiation

"[I]n cases where the patentee's theory of equivalents would 'entirely vitiate a particular claim element, partial or complete summary judgment should be rendered by the court.'" *Sage Products, Inc., v. Devon Industries, Inc.*, 126 F.3d 1420, 1429 (Fed. Cir. 1997) (citation omitted). The doctrine of vitiation or the "all elements" rule forecloses a patentee's resort to the doctrine of equivalents when the facts or theories presented in a case would completely read a limitation out of a claim because "all elements" of a claim must be present in an accused product for there to be infringement. *See Depuy Spine*, 469 F.3d at 1017.

Dr. Reddy's argues that the amended (and limiting) term pemetrexed disodium would be read out of the claim and restored with the rejected term "antifolates" under Lilly's theory of equivalents as articulated in its expert reports. Lilly responds that its theory on the scope of equivalents does not encompass all antifolates; rather, Lilly poses the function-way-result test to prove that the two products are equivalent in the context of the claimed treatment claims because they both involve pemetrexed treatment that results in a chemotherapy effect. The dispute between the parties on this issue includes a discussion of Lilly's expert, Dr. Bruce A. Chabner's ("Dr. Chabner"), report and deposition. Dr. Reddy's contends that Dr. Chabner raises new theories on defining the function-way-result test in his deposition which were not raised in his expert report that are inadmissible at trial and at the summary judgment stage. (Filing No. 167 at 16). Specifically, Dr. Reddy's argues that Dr. Chabner changed his "way" analysis

from "inhibition of [] folate-dependent enzymes" to "inhibition of *particular* folate-dependent enzymes." *Id*. at 16. (emphasis added). Previously, the Court ruled that Dr. Chabner's report and deposition were admissible when the Court sustained Lilly's objection to the Magistrate Judge's striking portions of this evidence as well as Lilly's literal infringement theory. (Filing No. 154.) Additionally, the factual record on the distinction between pemetrexed disodium and pemetrexed ditromethamine precludes summary judgment as it presents a clear battle of the experts issue. The different salt form that is used between the two products goes directly to the heart of Lilly's doctrine of equivalents claim and the limitation is thus not entirely vitiated by the substitution. Because there are factual issues precluding summary judgment on the doctrine of equivalents and Lilly has met its burden in clearing the threshold issues raised by Dr. Reddy's, summary judgment is not warranted.

D. Indirect 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). Because Dr. Reddy's does not provide care to patients the direct infringement is attributed to the healthcare providers. 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).

The Court will address liability for inducement of infringement first. "Liability for inducement of infringement is predicated on a finding of direct infringement by a third party." *Eli Lilly and Co. v. Teva Parenteral Medicines, Inc.*, 126 F. Supp. 3d 1037,

1041 (S.D. Ind. 2015) (citing *Limelight Networks v. Akamai Technologies Inc.,* 134 S.Ct. 2111, 2117 (2014)). "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).

Liability for contributory infringement under 35 U.S.C. § 271(c) can be avoided if the product is a "staple article or commodity of commerce suitable for substantial noninfringing use." "One who makes and sells articles which are only adapted to be used in a patented combination will be presumed to intend the natural consequences of his acts; he will be presumed to intend that they shall be used in the combination of the patent." *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.* 545 U.S. 913, 932 (2005).

Reviewing the record in a light most favorable to Lilly, Lilly has shown that Dr. Reddy's product will result in induced or contributory infringement. With regards to the literal infringement theory and

cisplatin use, Lilly argues that standard practice would require healthcare providers to use saline solution with cisplatin which would then result in a solution containing pemetrexed and disodium ions—*i.e.* pemetrexed disodium. Specific, knowing intent is required for inducement and contributory infringement. Nevertheless, Lilly has shown there are disputed issues of material fact on whether Dr. Reddy's label instructs an infringing use under either literal infringement or the doctrine of equivalents to infer intent and knowledge necessary for either form of indirect infringement. "Even where a proposed label does not explicitly track the language of a claimed method, a package insert containing directives that will 'inevitably lead some consumers to practice the claimed method' provides sufficient evidence for a finding of specific intent." *Sanofi v. Glenmark Pharmaceuticals Inc., USA*, 204 F. Supp. 3d 665, 673-74 (D. Ct. Del.) (quoting *AstraZeneca*, 633 F. 3d at 1060). 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."). Viewing the facts in the light most favorable to Lilly, it has shown that Dr. Reddy's label will instruct users to perform the patented method by inducing or contributing to infringement and that Dr. Reddy's had the requisite intent and knowledge that its label

would cause such infringement. Thus, summary judgment is precluded.

IV. CONCLUSION

There are genuine disputes of material fact with respect to the claims before the Court. For the reasons stated above, Dr. Reddy's Motion for Summary Judgment (Filing No. 132) is DENIED. Lilly's literal infringement and doctrine of equivalents claims remain pending for trial.

SO ORDERED.

Date: 12/14/2017

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