No. _____

IN THE
Supreme Court of the United States

HOSPIRA, INC.,
Petitioner,
v.
ELI LILLY AND COMPANY,
Respondent.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTIORARI

SARA TONNIES HORTON
YUSUF ESAT
JENNER & BLOCK LLP
353 N. Clark St.
Chicago, IL 60654

ADAM G. UNIKOWSKY
Counsel of Record
JENNER & BLOCK LLP
1099 New York Ave., NW
Suite 900
Washington, DC 20001
(202) 639-6000
aunikowsky@jenner.com

QUESTION PRESENTED

This Court has long recognized the doctrine of prosecution history estoppel, which provides that when a patentee narrows a claim during patent prosecution for a "substantial reason related to patentability," "the court should presume that the patentee surrendered all subject matter between the broader and the narrower language," and therefore may not reclaim that subject matter under the doctrine of equivalents. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 740 (2002). In *Festo*, this Court held that "[t]here are some cases, however, where the amendment cannot reasonably be viewed as surrendering a particular equivalent." *Id.* at 740. One such scenario arises when "the rationale underlying the amendment may bear no more than a tangential relation to the equivalent in question." *Id.* The Court then went on to hold that "[t]he patentee must show that at the time of the amendment one skilled in the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent." *Id.* at 741.

The question presented is:

Whether a patentee may recapture subject matter via the doctrine of equivalents under the "tangential relation" exception by arguing that it surrendered more than it needed to during prosecution to avoid a prior art rejection, even if a claim could reasonably have been drafted that would literally have encompassed the alleged equivalent.

CORPORATE DISCLOSURE STATEMENT

Petitioner Hospira, Inc. is an indirect, wholly-owned subsidiary of Pfizer Inc. As to Pfizer Inc., it has no parent corporation and no publicly held corporation holds 10% or more of its stock.

STATEMENT OF RELATED CASES

Eli Lilly & Co. v. Hospira, Inc., Nos. 2018-2126 and 2018-2127 (Fed. Cir.) (Federal Circuit case below).

Eli Lilly & Co. v. Hospira, Inc., No. 1:16-cv-03460-TWP-MPB (S.D. Ind.) (District Court case below).

The following case was a companion case in the Federal Circuit: *Eli Lilly & Co. v. Dr. Reddy's Labs., Ltd.*, No. 2018-2128 (Fed. Cir.). The Federal Circuit decided that appeal in the same opinion as the appeal at issue in this petition, although separate judgments were issued in each appeal. That case arose from the following district court case: *Eli Lilly & Co. v. Dr. Reddy's Labs., Ltd.*, No. 1:16-cv-00308-TWP-MPB (S.D. Ind.).

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PETITION FOR WRIT OF CERTIORARI

Hospira, Inc. petitions for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit.

OPINIONS BELOW

The decision of the Federal Circuit (Pet. App. 1a-31a) is reported at 933 F.3d 1320. The order of the Federal Circuit denying rehearing en banc (Pet. App. 48a-49a) is unreported. The decision of the Southern District of Indiana (Pet. App. 32a-47a) is reported at 2018 WL 3008570.

JURISDICTION

The judgment of the Federal Circuit was entered on August 9, 2019. The order of the Federal Circuit denying rehearing en banc was entered on November 8, 2019. On January 28, 2020, the Chief Justice granted Hospira's application (No. 19A841) extending the time to file this petition for certiorari until February 24, 2020. This Court has jurisdiction pursuant to 28 U.S.C. § 1254.

INTRODUCTION

This case concerns the patent law doctrine of prosecution history estoppel. This Court last addressed that doctrine in *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722 (2002). Relying on isolated words in *Festo*, the Federal Circuit has constructed a doctrinal framework governing prosecution history estoppel that is untethered from *Festo*'s reasoning and will lead to abuse of the patent prosecution process. This Court

should grant certiorari and restore order to that doctrine.

Prosecution history estoppel is a limitation on the patent law doctrine known as the doctrine of equivalents. The doctrine of equivalents provides that "a product or process that does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chemical Co.*, 520 U.S. 17, 21 (1997). The doctrine of equivalents exists because "the nature of language makes it impossible to capture the essence of a thing in a patent application." *Festo*, 535 U.S. at 731. Thus, "[t]he language in the patent claims may not capture every nuance of the invention or describe with complete precision the range of its novelty." *Id.* "If patents were always interpreted by their literal terms, their value would be greatly diminished. Unimportant and insubstantial substitutes for certain elements could defeat the patent, and its value to inventors could be destroyed by simple acts of copying." *Id.*

The doctrine of prosecution history estoppel applies when a patentee submits a patent application with broad claim language, and then narrows that claim language during patent prosecution, thus surrendering a portion of the subject matter covered by the original version of the claim. That doctrine provides that if a product or process *is* literally covered by the original, broader version of the claim, but *is not* literally covered by the final, narrower version of the claim, then the

patentee is generally estopped from asserting that the product or process infringes the claim under the doctrine of equivalents.

This Court explained the basis for prosecution history estoppel in *Festo*:

> Prosecution history estoppel ensures that the doctrine of equivalents remains tied to its underlying purpose. Where the original application once embraced the purported equivalent but the patentee narrowed his claims to obtain the patent or to protect its validity, the patentee cannot assert that he lacked the words to describe the subject matter in question. The doctrine of equivalents is premised on language's inability to capture the essence of innovation, but a prior application describing the precise element at issue undercuts that premise. In that instance the prosecution history has established that the inventor turned his attention to the subject matter in question, knew the words for both the broader and narrower claim, and affirmatively chose the latter.

Id. at 734-35.

The general rule of prosecution history estoppel is subject to certain exceptions. One exception, not at issue in this case, applies when "the patent holder demonstrates that an amendment required during prosecution had a purpose unrelated to patentability." *Warner-Jenkinson*, 520 U.S. at 40-41.

In *Festo*, this Court addressed the scenario where, as here, a patentee *does* amend a patent claim during

prosecution for a purpose related to patentability. This Court declined to hold that there was a "complete bar" on asserting the doctrine of equivalents in that scenario. 535 U.S. at 740.

Instead, the Court held that a "court should presume that the patentee surrendered all subject matter between the broader and the narrower language," and "the patentee should bear the burden of showing that the amendment does not surrender the particular equivalent in question." *Id.* In imposing this burden on the patentee, the Court emphasized that "[t]he patentee, as the author of the claim language, may be expected to draft claims encompassing readily known equivalents." *Id.* But the Court also concluded that "[t]here are some cases, however, where the amendment cannot reasonably be viewed as surrendering a particular equivalent." *Id.* The Court explained:

> 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 a finding of equivalence.

Id. at 740-41. In the next paragraph, the Court summarized its holding as follows: "The patentee must show that at the time of the amendment one skilled in

the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent." *Id.* at 741.

In the 18 years since *Festo* was decided, the Federal Circuit has hardened the above-quoted paragraph into a three-part test, in which a patentee may refute the presumption of prosecution history estoppel via either the "unforeseeable" exception; the "tangential relation" exception; or the "some other reason" exception. *See, e.g.*, *Honeywell Int'l, Inc. v. Hamilton Sundstrand Corp.*, 523 F.3d 1304, 1310-11 (Fed. Cir. 2008) (quotation marks omitted).

This case concerns the "tangential relation" exception, or, as it has become known, the doctrine of "tangentiality." Pet. App. 20a, 25a. The Federal Circuit's tangentiality jurisprudence has gone seriously awry. Specifically, the Federal Circuit now holds that even when the patentee indisputably *could* "reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent," *Festo*, 535 U.S. at 741, the doctrine of prosecution history estoppel applies so long as the patentee can show that its purpose for an amendment is sufficiently disconnected from its theory of equivalence. That holding is irreconcilable with *Festo*'s rationale. And it unfairly skews the patent playing field in favor of patentees, by artificially expanding the scope of patent monopolies and handcuffing the ability of competitors to design their products in a manner that avoids infringement.

The straightforward facts of this case illustrate the Federal Circuit's fundamental misunderstanding of

Festo. Respondent Eli Lilly & Co. ("Lilly") submitted a patent application to the Patent Office that included claims with the broad claim term "antifolate." Those claims were rejected as anticipated or obvious in light of prior art. Lilly then narrowed the claim term "antifolate" to one particular type of antifolate—"pemetrexed disodium." The claims were subsequently allowed by the Patent Office.

Lilly sued Petitioner Hospira, Inc. ("Hospira") for patent infringement. Hospira's product uses a different pemetrexed compound—pemetrexed ditromethamine. Because pemetrexed ditromethamine is a type of antifolate, it would have literally fallen within the original version of the claim. But because pemetrexed ditromethamine is different from pemetrexed disodium, it does not literally fall within the final version of the claim. Therefore, unless an exception applies, prosecution history estoppel bars Lilly from asserting infringement under the doctrine of equivalents.

This case should have been easy: no exception applies, and prosecution history estoppel bars Lilly from asserting its claim. There would have been a straightforward way for Lilly to narrow its claim in a manner that would have encompassed the alleged equivalent. It could have simply said "pemetrexed and its salts," or "all pemetrexed compounds," or similar language, rather than limiting its claim to one particular pemetrexed compound. This was emphatically not a case in which the patentee "lacked the words to describe the subject matter in question." *Festo*, 535 U.S. at 734. Thus, prosecution history estoppel should have applied: Lilly could not "show that

at the time of the amendment one skilled in the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent," as *Festo* requires. *Id.* at 741.

But the Federal Circuit took a different view. In its view, Lilly's subjective *goal* in amending its claim was to distinguish pemetrexed compounds from other antifolates, not to distinguish one pemetrexed compound from another. The Federal Circuit reasoned that Lilly *could have* achieved that subjective goal in a different way—merely by narrowing the claim to "pemetrexed compounds," rather than to one particular pemetrexed compound. Therefore, the Federal Circuit elected to treat the claim as though Lilly actually *did* narrow its claim to all pemetrexed compounds, rather than pemetrexed disodium. Specifically, it held that pemetrexed *ditromethamine* could infringe a claim limited, by its terms, to pemetrexed *disodium*—thus nullifying Lilly's decision during prosecution to narrow its claim to pemetrexed disodium.

The Federal Circuit's decision warrants this Court's review. If the Federal Circuit's decision stands, the public notice function of patent claiming and patent prosecution will be nullified. Where, as here, a patent applicant elects to narrow a claim in such a way that unambiguously *excludes* a class of compounds, both the patent office and the public should be able to rely on that election and infer that the excluded class of compounds is non-infringing. Yet under the Federal Circuit's decision, patent applicants can play bait-and-switch games with the patent office—making the strategic decision to narrow a claim during prosecution,

then expanding the claim via the doctrine of equivalents by making post-hoc arguments about the *reason* for that narrowing. The Court should reverse the Federal Circuit and prevent the abuse of the patent prosecution process that the Federal Circuit's decision portends.

STATEMENT

Lilly is a pharmaceutical company that markets a lung cancer drug under the trade name ALIMTA. Pet. App. 4a. ALIMTA is composed of a chemical compound known as pemetrexed disodium. *Id.* Pemetrexed disodium is a type of salt, composed of one pemetrexed molecule bonded with two sodium atoms. Pet. App. 4a, 15a.

Pemetrexed is a type of antifolate. Pet. App. 4a. It is structurally similar to folic acid and competitively binds to certain enzymes that use folic acid as cofactors in nucleotide synthesis. *Id.* Unlike folic acid, it inhibits rather than enables synthesis of those nucleotides. *Id.* Thus, it is an "antifolate"—it counteracts the effect of folic acid on nucleotide synthesis. *Id.* In doing so, it slows down the growth and division of cancer cells. Pet. App. 5a. Pemetrexed has been widely known for decades and is not under patent protection. *Id.*

This case concerns U.S. Patent No. 7,772,209, owned by Lilly ("the '209 patent"). The '209 patent is directed not to pemetrexed itself, but instead to a particular type of treatment technique that uses pemetrexed disodium in conjunction with other chemical compounds in order to combat cancer. Claim 12 is representative:

> **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.

Pet. App. 7a. The specification explains that this treatment method lessens antifolate toxicity without sacrificing efficacy. Pet. App. 6a.

Lilly originally, but unsuccessfully, sought patent protection for a broader patent claim. The '209 patent descends from U.S. Patent Application 10/297,821 ("the '821 application"). Pet. App. 8a. That application sought patent protection for a claim covering the use of *any* antifolate, rather than just pemetrexed disodium. In particular, the '821 application originally included the following independent claims:

> 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.

Pet. App. 8a. These claims are broader than the final version of the claim. They encompass *any* antifolate (rather than just pemetrexed disodium) and *any* methylmalonic acid lowering agent (rather than just Vitamin B12 in particular quantities). As well, claim 5 covers *any* FBP binding agent (rather than just folic acid).

As relevant here, original claim 2 was rejected in view of a 1978 reference known as Arsenyan, while original claim 5 was rejected in view of the combination of Arsenyan and other references. Pet. App. 8a-9a. Arsenyan disclosed experiments treating mice with tumors using the combination of methotrexate—an antifolate—and a methylmalonic acid lowering agent known as methylcobalamin. Pet. App. 8a.

In response, Lilly amended its claims. It replaced the broader term "antifolates" with the narrower term "pemetrexed disodium." Pet. App. 9a. And, it argued to the Examiner that "[t]here is no disclosure in Arsenyan et al. of the invention as presently claimed" because Arsenyan "does not disclose pemetrexed disodium and does not disclose the use of vitamin B12 or a pharmaceutical derivative to reduce the toxicity associated with the administration of pemetrexed

disodium." Hospira Opening C.A. Br. at 10 (quoting Appx430); Pet. App. 9a. The Examiner withdrew his objections based on Arsenyan and the claims ultimately progressed to allowance. Pet. App. 9a.

After the patent was allowed by the Patent Office, Lilly began suing its competitors for infringement, leading to extensive litigation. In an initial round of litigation, Lilly sued competitors for infringement based on its competitors' efforts to sell the drug actually recited in the claim: pemetrexed disodium. *See Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357 (Fed. Cir. 2017).

This case concerns Lilly's effort to enforce its patent against competitors who do not seek to sell pemetrexed disodium. In 2016, Hospira submitted to the FDA a New Drug Application ("NDA") for a pemetrexed ditromethamine product. That molecule consists of one pemetrexed molecule bonded with two tromethamine molecules. Pet. App. 10a.

Lilly sued Hospira for infringement in the Southern District of Indiana. Pet. App. 10a. As relevant here, Lilly argued that an NDA based on pemetrexed ditromethamine infringed, via the doctrine of equivalents, a claim reciting pemetrexed disodium.[1]

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[1] Lilly also argued, and the District Court agreed, that Hospira literally infringed because pemetrexed ditromethamine was dissolved in a saline solution (*i.e.*, a solution containing sodium). Pet. App. 38a-39a. The Federal Circuit, however, reversed that portion of the District Court's holding. Pet. App. 16a ("There is no dispute that

Hospira countered that prosecution history estoppel barred Lilly's claim under the doctrine of equivalents. Hospira reasoned that Lilly's originally-submitted patent claim sought protection for a claim encompassing all "antifolates," but Lilly amended that claim by narrowing "antifolates" to "pemetrexed disodium." Thus, because pemetrexed ditromethamine literally fell within the original version of the claim (because it is an antifolate), but did not literally fall within the final version of the claim (because it is not pemetrexed disodium), Lilly was estopped from asserting that Hospira infringed under the doctrine of equivalents. The District Court rejected Hospira's argument, holding that Lilly had rebutted the presumption of prosecution history estoppel because "the rationale underlying the amendment may bear no more than a tangential relation to the equivalent in question." Pet. App. 40a-43a; *see Festo*, 535 U.S. at 740.

The Federal Circuit consolidated Hospira's appeal with a different, similar appeal involving a different party (Dr. Reddy's Laboratories), and affirmed in relevant part. The Federal Circuit acknowledged Lilly's concession that "the amendment in question was both narrowing and made for a substantial reason

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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.").

relating to patentability." Pet. App. 19a. Thus, Lilly conceded that a presumption of prosecution history estoppel applied, and that Lilly bore the burden of rebutting that presumption. *Id.*; *see* Lilly C.A. Br. at 48. The sole issue in the case was whether Lilly had successfully rebutted that presumption by showing that the "rationale of its amendment '[b]ore no more than a tangential relation to the equivalent in question.'" Pet. App. 19a (quoting *Festo*, 535 U.S. at 740).

The court held that Lilly had met that burden. In its view, the "reason for Lilly's amendment … was to narrow original claim 2 to avoid Arsenyan, which only discloses treatments using methotrexate, a different antifolate." Pet. App. 20a-21a. "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." Pet. App. 21a.

Of course, the amended claim did not recite a method of administering *pemetrexed*; it recited a method of administering *pemetrexed disodium*. But the Federal Circuit brushed this point off: "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." Pet. App. 23a. The court quoted the statement in *Festo* that an amended claim need not "become[] so perfect in its description that no one could devise an equivalent." *Id.*

(quoting *Festo*, 535 U.S. at 738). The court deemed the "less sweeping and more sensible reason for Lilly's amendment" to be "to surrender antifolates other than pemetrexed." Pet. App. 26a.

REASONS FOR GRANTING THE WRIT

In *Festo*, this Court held that when a patentee narrows a claim during prosecution, "the court should presume that the patentee surrendered all subject matter between the broader and the narrower language." 535 U.S. at 740. But "[t]here are some cases, however, where the amendment cannot reasonably be viewed as surrendering a particular equivalent." *Id.* One such case occurs when "the rationale underlying the amendment may bear no more than a tangential relation to the equivalent in question." *Id.* In the next paragraph, the Court summarized its holding as follows: "The patentee must show that at the time of the amendment one skilled in the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent." *Id.* at 741.

The question in this case is straightforward: when the record makes clear that the patentee *could* reasonably have been expected to have drafted a claim that would have literally encompassed the alleged equivalent, can the patentee nonetheless take refuge in the "tangential relation" exception? The answer should be no. In reaching a contrary conclusion, the Federal Circuit's decision contravened the plain language of this Court's decision, and its decision will seriously jeopardize the integrity of the patent prosecution

process. The Court should grant certiorari and reverse.

I. The Federal Circuit's Decision Is Wrong.

Begin with what is plain from the record: this is not a case where the patentee "could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent." *Festo*, 535 U.S. at 741. Lilly cannot conceivably claim that—in *Festo*'s words—it "lacked the words to describe the subject matter in question." *Id.* at 734-35. Lilly could have simply said "pemetrexed and its salts," or "pemetrexed compounds," or similar language. If it had done so, pemetrexed ditromethamine would have literally infringed. Indeed, *Lilly's own prior patent* defined "pemetrexed" as "the stable salts, acids and free base forms thereof."[2] If Lilly had simply reused its own language from its own prior patent, infringement would be clear.

Nor can Lilly conceivably claim that it "could not reasonably be expected to have drafted" a broader claim because it could not have foreseen that a competitor might use a different pemetrexed compound. *Festo* holds that prosecution history estoppel does not apply when the equivalents were "unforeseeable at the time of the amendment and beyond a fair interpretation of what was surrendered." 535 U.S. at 738. But Lilly expressly declined to rely on

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[2] Hospira Opening C.A. Br. at 3 (quoting Appx1397); *see* U.S. Patent No. 6,686,365, at 3:10-20.

Festo's "unforeseeability" exception below, Lilly C.A. Br. at 52 n.11, and the Federal Circuit never suggested it was satisfied.

From the Federal Circuit's perspective, none of this mattered. The dispositive point, in the Federal Circuit's view, was that the *purpose* of Lilly's amendment was "to more accurately define what it actually invented, an improved method of administering pemetrexed." Pet. App. 21a. Thus, it deemed the "less sweeping and more sensible reason for Lilly's amendment" to be "to surrender antifolates other than pemetrexed." Pet. App. 26a. In other words, because Lilly *could* have achieved its purpose of overcoming the prior art by limiting its claim to "pemetrexed compounds" or similar language, it was irrelevant that Lilly instead decided to limit its claim all the way to "pemetrexed disodium."

The Federal Circuit's interpretation of *Festo* was incorrect—and its error was not simply a misapplication of *Festo* to the facts of this case. It reflects a basic misunderstanding of the doctrine of prosecution history estoppel.

Festo holds that in some cases, "the rationale underlying the amendment may bear no more than a tangential relation to the equivalent in question." 535 U.S. at 740. Contrary to the Federal Circuit's conclusion, that sentence is not a freestanding invitation for courts to apply an exception to prosecution history estoppel whenever they perceive that the patentee's reason for an amendment did not require the patentee to surrender the claimed equivalent.

Instead, as this Court made clear in the very next paragraph of *Festo*, the "tangential relation" exception is simply one *example* of the scenario in which "one skilled in the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent." *Id.* at 741. And that scenario, in turn, reflects the core purpose of the doctrine of equivalents: to ensure that the patentee may receive the full benefit of his invention even when "he lacked the words to describe the subject matter in question." *Id.* at 734. Thus, under *Festo*, the patentee's ultimate burden is to demonstrate that it could not reasonably have amended the claim so as to encompass the claimed equivalent. *Festo*'s reference to the "tangential relation" exception reflects the fact that, in appropriate cases, that ultimate burden can be *satisfied* by establishing the "tangential relation" between the amendment and the equivalent. But it does not *relax* that ultimate burden. And Lilly cannot overcome that burden, because it so plainly could have amended its claim so as to encompass the claimed equivalent.

The Federal Circuit's decision boiled down to its theory that Lilly did not *have* to limit its claim all the way down to "pemetrexed disodium," to overcome the prior art—"pemetrexed compounds," or the like, would have been enough—and therefore, Lilly should be relieved of the consequences of its choice during prosecution. But prosecution history estoppel exists to protect the *public*, not the *patentee*. And prosecution history estoppel should apply because any rational member of the public would interpret Lilly's amendment to be a conscious effort to limit its claim to

a particular compound, regardless of Lilly's purpose in making the amendment.

Consider the following example. A claim in a patent application recited "fruit," and then, in response to a rejection, the claim was amended to "Red Delicious apples." Anyone would infer that the amendment excludes other types of apples. Otherwise, the patentee would have just said "apples." Thus, prosecution history estoppel should bar a patentee from accusing Honeycrisp apples of infringement. Under the Federal Circuit's decision, however, a patentee could later accuse Honeycrisp apples of infringement. It could reason as follows: the prior art that gave rise to the rejection referred only to bananas. As such, the patentee did not *need* to narrow its claim to "Red Delicious apples," and *could* have narrowed its claim to "apples." And so—notwithstanding its voluntary choice to narrow its claim to "Red Delicious apples"—the court can simply pretend that the patentee *actually* narrowed its claim to "apples." That has to be wrong—and for the same reason, the Federal Circuit's decision is wrong too. By narrowing its claim from "antifolates" to "pemetrexed disodium," Lilly told the public that its claim was limited to "pemetrexed disodium." The public should have the right to rely on that, regardless of whether Lilly *could* have narrowed its claim to "pemetrexed" if it had been so inclined.

In the decision below, the Federal Circuit asserted that *Festo* supported its decision—but its discussion of *Festo* demonstrates its misunderstanding of that case. The Federal Circuit brushed off the fact that Lilly gratuitously limited its claim to pemetrexed disodium

with the following statement: "We do not demand perfection from patent prosecutors, and neither does the Supreme Court." Pet. App. 23a. As support for this proposition, the Federal Circuit quoted the following statement from *Festo*: "It does not follow, [however,] that [the] amended claim becomes so perfect in its description that no one could devise an equivalent." *Id.* (quoting *Festo*, 535 U.S. at 738).

But the Federal Circuit failed to quote the very next sentence in *Festo*: "After amendment, as before, language remains an imperfect fit for invention." 535 U.S. at 738. And that sentence demonstrates the Federal Circuit's error. Under the Federal Circuit's decision, prosecution history estoppel does not apply even when language is a *perfect* fit for invention. Here, the Federal Circuit concluded that what Lilly "actually invented" was "an improved method of administering pemetrexed." Pet. App. 21a. There is *perfectly* clear language for that invention: "pemetrexed." Lilly's decision to narrow the claim to pemetrexed disodium reflected its own strategic decision—not any imperfection in language that warrants relaxing prosecution history estoppel.

The Federal Circuit's legal standard is wrong for a second reason. Under *Festo*, the "tangential relation" exception requires assessing whether the "rationale underlying the amendment" bears a "tangential relation to the equivalent in question." 535 U.S. at 740. The Federal Circuit's legal standard wrongly focuses on the reason for *amending the claim at all*, rather than the reason for the *particular amendment that the*

patentee made—which should have been the inquiry dictated by *Festo*.

This case illustrates the flaw in the Federal Circuit's legal standard. Lilly amended "antifolates" to "pemetrexed disodium." The Federal Circuit thought that the question was: Why did Lilly make the amendment at all? And it answered that question: To overcome prior art that disclosed a different antifolate.

But the Federal Circuit should have asked a different question. It should have asked: why did Lilly use the words "*pemetrexed disodium*" in its amendment? Lilly's explanation for its amendment did not adequately respond to that question, because Lilly did not explain why it added the word "disodium." And if the Federal Circuit had posed the right question, it would have reached the right answer: prosecution history estoppel applies.

Lilly's decision to narrow the claim to "pemetrexed disodium" did not come out of nowhere. Rather, that decision reflects the fact that ALIMTA—the product Lilly sells—is pemetrexed disodium. Pet. App. 4a; *see* Lilly C.A. Br. at 61. So, in reality, Lilly had two reasons for its amendment: to overcome the prior art (which is why it amended its claim in the first place), and to limit its claim to the product it was selling (which is why it chose the particular words of the amendment: pemetrexed disodium). But the latter reason does *not* satisfy the "tangential relation" exception. The equivalence between pemetrexed disodium (the product Lilly sells), and pemetrexed ditromethamine (a product Lilly does not sell), has a

direct—not tangential—relation to an amendment limiting a claim to the product that Lilly sells.

Thus, the Federal Circuit's rule relieves patentees of the burden of showing that the rationale for the *particular amendment the patentee made* is tangential to the claimed equivalence. That rule is irreconcilable with *Festo*'s reasoning. Under *Festo*, "estoppel ensures that the doctrine of equivalents remains tied to its underlying purpose": to ensure patent protection even when the patentee "lacked the words to describe the subject matter in question," in view of "language's inability to capture the essence of innovation." *Festo*, 535 U.S. at 734-35. Given that purpose, *Festo* should be construed to require courts to examine the basis for the *amendment that the patentee chose*—not the reason for making the amendment at all. By examining the reason for the *particular* choice of amendment, the court can ensure, as *Festo* requires, that prosecution history estoppel applies when the patentee could reasonably have amended the claim to include the claimed equivalent. In ignoring the words that Lilly actually used in its amendment, the Federal Circuit ignored *Festo*'s core holding.

II. This Court Should Grant Certiorari And Reverse The Federal Circuit's Decision.

This case warrants Supreme Court review. The question presented recurs frequently and is important to the sound administration of American patent law. The Federal Circuit's rule will create significant uncertainty in the scope of patent claims—and the Federal Circuit's intra-circuit inconsistency on the "tangentiality" exception to prosecution history

estoppel will only make the situation worse. Finally, this case is an ideal vehicle.

A. This Case is Sufficiently Important to Warrant Supreme Court Review.

The Court should grant certiorari in view of the importance of the question presented to American patent law. Prosecution history estoppel generally, and the "tangential relation" exception specifically, are constantly litigated. The Federal Circuit's holding that courts should focus on the *purpose* of an amendment—rather than whether the patentee could reasonably have been expected to draft a claim encompassing the claimed equivalent—will thus have a significant and detrimental real-world effect. Worse, the Federal Circuit's decision will lead to gamesmanship in the Patent Office, as patentees narrow their claims during prosecution and then seek to expand their claims via the doctrine of equivalents by making post-hoc assertions about their rationales for the amendments. The Court should grant certiorari to prevent distortion of both patent litigation and patent prosecution, and ensure that the doctrine of equivalents does not unduly stifle the ability of competitors to design new products outside the scope of a patent claim.

It is an unfortunate but routine tactic for patentees to narrow claims during prosecution in the Patent Office and then, after the patent is allowed, attempt to re-broaden them in the courts via the doctrine of equivalents. As such, prosecution history estoppel is a constant source of litigation. Indeed, the single sentence fragment in *Festo* about the "tangential relation" exception has taken on a life of its own, as the

Federal Circuit and district courts constantly hear disputes about whether the so-called "tangentiality" exception is satisfied. *See, e.g.*, *Amgen Inc. v. Amneal Pharm. LLC*, 945 F.3d 1368, 1382 (Fed. Cir. 2020); *Pharma Tech Sols., Inc. v. LifeScan, Inc.*, 942 F.3d 1372, 1381-84 (Fed. Cir. 2019); *Ajinomoto Co. v. ITC*, 932 F.3d 1342, 1355 (Fed. Cir. 2019); *Water Tech., LLC v. Kokido Dev. Ltd.*, No. 4:17-cv-01906-AGF, 2020 WL 418549, at *6-7 (E.D. Mo. Jan. 27, 2020); *Qualcomm Inc. v. Apple Inc.*, No. 17cv1375, 2019 WL 448278, at *3 (S.D. Cal. Feb. 5, 2019); *Amgen Inc. v. Amneal Pharm. LLC*, 328 F. Supp. 3d 373, 395 (D. Del. 2018), *aff'd in part, rev'd in part*, 945 F.3d 1368 (Fed. Cir. 2020); *Bio-Rad Labs., Inc. v. 10X Genomics, Inc.*, 322 F. Supp. 3d 537, 543 (D. Del. 2018), *appeal docketed*, No. 19-2255 (Fed. Cir. Aug. 19, 2019); *Kenu, Inc. v. Belkin Int'l, Inc.*, No. 15-cv-01429-JD, 2018 WL 2445318, at *3 (N.D. Cal. May 31, 2018); *iCeutica Pty Ltd. v. Lupin Limited*, No. MJG-17-0394, 2018 WL 656447, at *9 (D. Md. Feb. 1, 2018). And in those cases, disputes like the one at issue in this case abound. As one example, three days before the decision below was released, the Federal Circuit issued a different decision holding that the "tangential relation" exception applied in view of its assessment of "the reason for the narrowing amendment," *Ajinomoto*, 932 F.3d at 1355, notwithstanding the dissenting judge's admonition that the court had "ignore[d] how the patentee deliberately elected to narrow the claims." *Id.* at 1363 (Dyk, J., dissenting).

The Federal Circuit's view of the "tangential relation" exception will significantly complicate that

abundant litigation. Even where, as here, it is clear that a patentee could reasonably have amended a claim so as to encompass a claimed equivalent, courts will be forced to plumb the prosecution history record to speculate on the true purpose of an amendment. Reverse-engineering a person's purpose is a famously difficult inquiry. And as addressed above, it is especially difficult in the context of prosecution history estoppel, because patentees may have dual purposes: one purpose for making the amendment at all, another purpose for amending the claim more narrowly than necessary to overcome the prior art. To apply the "tangential relation" exception, courts will have to determine which is the "right" purpose—an inquiry that is not only indeterminate, but disconnected from the doctrine's purposes.

Even worse, the Federal Circuit's decision will radically distort patent prosecution. It will encourage patentees to make strategic narrowing amendments, and eviscerate the public notice function of claim language and prosecution history.

Begin with the incentives for patent holders. Patent prosecution inevitably presents strategic considerations for patent applicants. Seek a patent that is too broad, and the Patent Office might reject it. Seek a patent that is too narrow, and the Patent Office might allow it—but competitors might be able to design around it. These strategic considerations become especially pertinent when the Patent Office rejects a claim in an application and demands that it be narrowed. In that scenario, the patent applicant faces a choice: either stand its ground and challenge the

rejection in court, or narrow the claim and make it less useful once it is allowed.

But the Federal Circuit's decision gives patent applicants a third choice: artificially narrow the patent so as to induce the Patent Office into allowing the patent, and then re-expand the patent after the fact via the doctrine of equivalents. Of course, the patent applicant needs to create a record showing that the reason for the amendment is "tangential" to the equivalents it will seek to sweep into its patent. But the patent applicant *itself* gets to write the prosecution history record, by making arguments to the Patent Office regarding the purpose of its amendments. And by strategically manipulating the prosecution history record, patentees can assert a patent that is broader than the Patent Office could ever have conceived.

This case illustrates the problem perfectly. Lilly originally asserted a claim directed to all antifolates. The Patent Office rejected that claim as overly broad. Lilly then narrowed its claim down to "pemetrexed disodium"—the drug it was manufacturing. In so doing, it made clear to the Patent Office that it was no longer seeking patent protection beyond the use of its own drug in the claimed treatment method. There was therefore no need for the Patent Office to determine whether Lilly was entitled to a broader patent that encompassed other pemetrexed compounds that it did not make.

Then, once it was awarded the patent, Lilly doubled back and asserted its claim against the very embodiments it disclaimed—embodiments that did not use pemetrexed disodium. The Federal Circuit blessed

this tactic, allowing Lilly to rely on Lilly's own carefully-worded statements in the prosecution history record to argue that the purported reason for the amendment was tangential to the claimed equivalent—and ignoring that the Patent Office had every right to rely on the *words of the amendment*, not just Lilly's carefully-worded arguments in support of the amendment.

The patent system should not work this way. In a properly functioning patent system, the Patent Office should be able to infer from a patentee's narrowing of a claim from a class of compounds to a single salt compound that the claim does not, in fact, stretch beyond that salt compound. But under the Federal Circuit's decision, it cannot. Rather, notwithstanding Lilly's representations to the Patent Office, the true scope of the patent actually extends to all pemetrexed compounds. And, according to the Federal Circuit, that is because Lilly's *arguments* in support of distinguishing the prior art are consistent with a hypothetical broader claim that would have used the word "pemetrexed compounds." The Federal Circuit's decision is an open invitation for future patentees to engage in similar bait-and-switch tactics with the patent office, allowing patentees to stretch their patents to cover products that the Patent Office had every reason to believe they would *not* cover.

The Federal Circuit's decision will also burden the public at large. Consider the matter from Hospira's perspective. The patent uses the phrase "pemetrexed disodium." Hospira did the right thing: It designed its product so as not to use pemetrexed disodium. The

prosecution history record shows that Lilly first wanted to assert its patent against all antifolates, but then narrowed its claim to the use of the drug it was manufacturing. This underscored Hospira's reasonable conclusion that if it used a drug that Lilly was not manufacturing that did not fall within the claim language, it would not infringe.

Yet the Federal Circuit found that Hospira *is* an infringer, on the theory that Hospira should have studied the interplay between Lilly's amendment and its arguments in support of the amendment and reverse-engineered that the "less sweeping and more sensible reason for Lilly's amendment" was "to surrender antifolates other than pemetrexed." Pet. App. 26a. If this holding stands, no claim or prosecution history record will ever be clear enough to foreclose infringement litigation ever again. This outcome will improperly expand the scope of a patentee's monopoly and will lead to a drag on innovation, as would-be innovators will be deterred from developing products that plainly fall outside the literal scope of patent claims that were intentionally narrowed during prosecution.

B. The Federal Circuit's Internal Inconsistency Will Exacerbate the Confusion over the Scope of Patent Claims.

There is an additional reason the Federal Circuit's decisions will spawn uncertainty on the scope of patent claims: the Federal Circuit itself is internally inconsistent on the scope of the "tangentiality" exception.

As explained above, the Federal Circuit concluded that because Lilly *could* have overcome the prior art by narrowing its claim to "pemetrexed compounds," Lilly would be treated *as if* it had narrowed its claim to "pemetrexed compounds." Lilly's argument that it did not *need* to amend its claim so as to exclude pemetrexed ditromethamine was deemed sufficient to show that the amendment was tangential to the equivalence between pemetrexed ditromethamine and pemetrexed disodium.

Yet the Federal Circuit has repeatedly rejected that exact argument. In *Norian Corp. v. Stryker Corp.*, 432 F.3d 1356 (Fed. Cir. 2005), for instance, the patentee amended a claim limitation from "sodium phosphate solution" (which was broad enough to include solutions containing multiple sodium phosphate solutes) to "a solution consisting of water and a sodium phosphate" (which only encompassed solutions containing a single sodium phosphate solute). *Id.* at 1361. In an effort to avoid prosecution history estoppel, the patentee made the identical argument that Lilly made here: "Because the sole purpose of the amendment was to avoid the effect of the [prior art], … the prosecution history should not be interpreted as disclaiming pure solutions that are made from more than a single solute." *Id.* The Federal Circuit disagreed, in language that could have been written for this case:

> The problem with that argument is that there is no principle of patent law that the scope of a surrender of subject matter during prosecution is limited to what is absolutely necessary to

> avoid a prior art reference that was the basis for an examiner's rejection. To the contrary, it frequently happens that patentees surrender more through amendment than may have been absolutely necessary to avoid particular prior art. In such cases, we have held the patentees to the scope of what they ultimately claim, and we have not allowed them to assert that claims should be interpreted as if they had surrendered only what they had to.

Id. at 1361-62.

Norian itself did not expressly consider the scope of the "tangential" exception, but a series of Federal Circuit cases have applied the same reasoning to the "tangential" exception. In *Felix v. American Honda Motor Co.*, 562 F.3d 1167 (Fed. Cir. 2009), for instance, the patentee added two limitations—one related to a channel, and one related to a gasket—to overcome prior art. In an effort to avoid prosecution history estoppel, the patentee made essentially the identical argument that Lilly made here—that it did not *need* to add the gasket limitation to overcome the prior art, and therefore should be treated as though it actually *did not* add that limitation. The Federal Circuit disagreed: "If Felix had intended only to add a channel and not add a gasket, he could easily have simply" done so. *Id.* at 1184; *see also, e.g.*, *Integrated Tech. Corp. v. Rudolph Techs., Inc.*, 734 F.3d 1352, 1358 (Fed. Cir. 2013) (rejecting application of "tangential" exception and stating: "It may be that [the patentee] did not need to surrender [territory] … to overcome [prior art]. The dispositive fact is that [the patentee] chose to do so.");

Chimie v. PPG Indus. Inc., 402 F.3d 1371, 1383 (Fed. Cir. 2005) (rejecting argument that "equivalents not within the prior art must be tangential to the amendment").

In the decision below, the Federal Circuit attempted to distinguish this line of cases with the following conclusory statement: "[T]he 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." Pet. App. 22a. Yet that statement does not offer any coherent guidance on when the Federal Circuit will accept a "buyer's remorse" defense and when it will not. Here, Lilly easily could have narrowed its claim to "pemetrexed compounds" rather than "pemetrexed disodium"; whether that fact is deemed dispositive for purposes of prosecution history estoppel appears to turn on the random draw of Federal Circuit panel. This Court's guidance on the scope of *Festo*'s "tangentiality" exception is therefore urgently needed.

C. This Case Is The Ideal Vehicle.

This case is the ideal vehicle to address the scope of *Festo*'s "tangentiality" exception. The facts are remarkably stark. Lilly narrowed its claim to "pemetrexed disodium," but later experienced buyer's remorse and argued that what it *really* meant to do was narrow its claim to all pemetrexed salts. The Federal Circuit allowed Lilly to evade the consequence of its choice and expand its claim after the fact to encompass all pemetrexed salts. If prosecution history estoppel exists to protect patentees who "lacked the

words to describe the subject matter in question," *Festo*, 535 U.S. at 734-35, then Lilly cannot possibly prevail. This case therefore presents the perfect opportunity for this Court to decide whether a patentee can assert prosecution history estoppel even when a claim could reasonably have been written that would have encompassed the claimed equivalent.

Moreover, awaiting additional Federal Circuit jurisprudence on the "tangentiality" exception would serve no purpose. The legal standard for prosecution history estoppel does not come from a statute; it comes from *Festo*, a decision from this Court. The dispute in this case centers around the relationship between two different statements in *Festo*: the statement recognizing the "tangential relation" exception, and the statement that prosecution history estoppel applies only when a claim could not have been reasonably written to encompass a claimed equivalent. Only this Court can authoritatively clarify what statements in this Court's own prior opinion mean. Two decades after *Festo*, it is time again for this Court to intervene.

The Federal Circuit's jurisprudence on prosecution history estoppel is not faithful to *Festo* and will complicate litigation and harm innovation. The Court should grant certiorari and reverse the Federal Circuit's errant holding.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted,

SARA TONNIES HORTON
YUSUF ESAT
JENNER & BLOCK LLP
353 N. Clark Ave
Chicago, IL 60654

ADAM G. UNIKOWSKY
Counsel of Record
JENNER & BLOCK LLP
1099 New York Ave., NW
Suite 900
Washington, DC 20001
(202) 639-6000
aunikowsky@jenner.com

APPENDIX

Appendix A

United States Court of Appeals
For the Federal Circuit

ELI LILLY AND COMPANY,
Plaintiff-Appellee

v.

HOSPIRA, INC.,
Defendant-Appellant

2018-2126, 2018-2127

Appeals from the United States District Court
For the Southern District of Indiana in
No. 1:16-cv-03460-TWP-MPB,
Judge Tanya Walton Pratt

ELI LILLY AND COMPANY,
Plaintiff-Appellee

v.

DR. REDDY'S LABORATORIES, LTD.,
DR. REDDY'S LABORATORIES, INC.,
Defendants-Appellants

2018-2128

Appeal from the United States District Court
For the Southern District of Indiana in
No. 1:16-cv-00308-TWP-MPB,
Judge Tanya Walton Pratt

Decided: August 9, 2019

ADAM LAWRENCE PERLMAN, Williams & Connolly, LLP, Washington, DC, argued for plaintiff-appellee in 2018-2126 and 2018-2128. Also represented by GALINA I. FOMENKOVA, DOV PHILIP GROSSMAN, DAVID M. KRINSKY, ANDREW P. LEMENS, CHARLES MCCLOUD; JAMES PATRICK LEEDS, Eli Lilly and Company, Indianapolis, IN.

BRADFORD PETER LYERLA, Jenner & Block LLP, Chicago, IL, argued for defendant-appellant in 2018-2126. Also represented by YUSUF ESAT, SARA TONNIES HORTON; ADAM G. UNIKOWSKY, Washington, DC.

JOHN C. O'QUINN, Kirkland & Ellis LLP, Washington, DC, argued for defendants-appellants in 2018-2128. Also represented by WILLIAM H. BURGESS, CALVIN ALEXANDER SHANK; JEFFERY B. ARNOLD, Holland & Knight LLP, Atlanta, GA; MERRI C. MOKEN, CHARLES A. WEISS, ERIC H. YECIES, New York, NY.

BRIAN TIMOTHY BURGESS, Goodwin Procter LLP, Washington, DC, for amicus curiae Actavis LLC in 2018-2128. Also represented by EDWINA CLARKE, EMILY L. RAPALINO, DARYL L. WIESEN, Boston, MA; LINNEA P. CIPRIANO, New York, NY.

Before LOURIE, MOORE, and TARANTO, *Circuit Judges.*

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

[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."

deoxythymidine 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[2,3d]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 antifolate 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 this

[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.*,

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*

Inc., 845 F.3d 1357 (Fed. Cir. 2017); *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 689 F.3d 1368 (Fed. Cir. 2012).

[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.

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 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, 68 S.Ct. 525, 92 L.Ed. 746 (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 noninfringement, *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 Kabushiki Co.*, 535 U.S. 722, 733, 122 S.Ct. 1831, 152 L.Ed.2d 944 (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, 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

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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 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 . . . .").

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 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 DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

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

ENTRY ON CROSS MOTIONS FOR SUMMARY JUDGMENT

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

below, the Court **grants** Lilly's Cross-Motion for Summary Judgment, and **denies** Hospira's Motion for Summary Judgment.

I. BACKGROUND

The '209 Patent describes a method of administering the chemotherapy drug, pemetrexed disodium, with a pretreatment regimen of vitamin B12 and folic acid (the "pretreatment regimen"), which is marketed by Lilly under the trade name ALIMTA®. The '209 Patent has been the subject of previous trials before this Court. *See Eli Lilly and Co. v. Teva Parenteral Medicines, Inc.*, 126 F. Supp.3d 1037, 1038 (S.D. Ind. 2015).[1] Two of those cases specifically concerned generic drug manufacturers that sought to market a generic version of ALIMTA® including labeling that induced physicians to direct patients to take folic acid and vitamin B_{12} in accordance with the pretreatment claims in the '209 Patent. Specifically, in the *Teva* case, the pretreatment regimen and whether the steps of the claimed method could be attributed to a single actor was at issue. *Id.* On February 1 and 2, 2018, this Court held a bench trial in *Eli Lilly & Co. v. Dr. Reddy's Laboratories, Ltd.*, No. 1:16-cv-308-TWP-MPB (the "Dr. Reddy's Case") involving primarily the same alleged infringing drug product at issue in this action: pemetrexed ditromethamine.[2]

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

[2] Because Hospira has conceded that many of the case-dispositive questions were all resolved against its interest in the Court's summary judgment ruling in the Dr. Reddy's Case, the Court relies

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

Similar to the issue in Dr. Reddy's Case, Hospira has also developed and designed a competing pemetrexed drug product, which uses a salt base, tromethamine, rather than the sodium base contained in Lilly's product.[4] Hospira seeks to market its product in the form of a new product that uses pemetrexed ditromethamine, unlike the generic drugs in previous trials before the Court. In large part, the issues in the present case and the Dr. Reddy's Case are the same. However, unlike Dr. Reddy's label, Hospira's label instructs that it can be reconstituted in saline solution (like ALIMTA®) in addition to 5% dextrose solution

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heavily on the analysis contained therein in resolving the present cross-summary judgment motion in this case. (*See* Filing No. 79-3.)

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

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

(like Dr. Reddy's product). (Filing No. 49-29; Filing No. 74-1 at 15-16.)

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

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

(Filing No. 1-1 at 9). The Court construed administration of pemetrexed disodium to refer to a liquid administration of pemetrexed disodium. (No. 1:16-308-TWP-MPB, ECF 199 at 9.) In the claim construction, the Court did not address the science of what happens when pemetrexed disodium is dissolved in aqueous solution in construing claim 12. *Id.* at 8-9. Nevertheless, Hospira and Lilly agree that based on the Court's construction in the Dr. Reddy's Case, that claim 12 would necessarily encompass any solution containing pemetrexed and sodium ions because it is undisputed that when pemetrexed disodium is dissolved in solution, pemetrexed disodium would not exist as an ionically bonded compound. (Filing No. 79 at 9; Filing No. 79-3 at 8). Rather the liquid solution contains pemetrexed and disodium (or tromethamine) ions disassociated from one another.[5] *Id.* Thus, the solution that is administered to the patient would not contain pemetrexed disodium as an ionically bonded salt, and instead would contain disassociated pemetrexed and sodium ions in solution. The Court directs the parties to the Dr. Reddy's Case for the analysis of the claim construction ruling, which binds the identical claim at issue in this case.

II. LEGAL STANDARD

The purpose of summary judgment is to "pierce the pleadings and to assess the proof in order to see whether there is a genuine need for trial." *Matsushita Electric Industrial Co. v. Zenith Radio Corp.*, 475 U.S. 574, 587

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

(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). This notion applies equally where, as here, opposing parties each move for summary judgment in their favor pursuant to Rule 56. *I.A.E., Inc. v. Shaver*, 74 F.3d 768, 774 (7th Cir. 1996).

III. DISCUSSION

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

A. Literal Infringement

"Literal infringement requires a patentee to prove by a preponderance of the evidence that every limitation of the asserted claim is literally met by the allegedly infringing device." *Biovail Corp. Intern. v. Andrx Pharmaceuticals, Inc.*, 239 F. 3d 1297, 1302 (Fed. Cir. 2001). Lilly contends that Hospira's product will literally infringe when it is reconstituted in saline according to Hospira's proposed labeling instructions. (Filing No. 79 at 18.) It is undisputed as manufactured pemetrexed ditromethamine is a separate, distinct compound from the claimed pemetrexed disodium. (Filing No. 74-1 at 24; Filing No. 79 at 18.) Thus, in solid form Hospira's product does not contain pemetrexed disodium. Hospira's product may be reconstituted and diluted pursuant to either saline preparation or dextrose preparation. (Filing No. 74-1 at 24.) Lilly contends that the saline preparation will literally infringe the '209 Patent.

Lilly has presented unrebutted expert testimony as to the chemical makeup of Hospira's product reconstituted in saline solution that would be administered to a patient. (Filing No. 78-1; Filing No. 78-2.) Additionally, Hospira concedes that under the

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

B. Doctrine of Equivalents

"The doctrine of equivalents extends the right to exclude beyond the literal scope of the claims." *Johnson & Johnston Associates, Inc. v. R.E. Service Co., Inc.*, 285 F.3d 1046, 1053 (Fed. Cir. 2002). "The doctrine of equivalents allows the patentee to claim those insubstantial alterations that were not captured in

drafting the original patent claim but which could be created through trivial changes." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 733 (2002). The doctrine of equivalents is restricted by the "all limitations" rule and the prosecution history estoppel rule by limiting the range of equivalents when claims have been narrowed. *See Pozen Inc. v. Par Pharmaceutical, Inc.*, 696 F.3d 1151, 1167. Hospira argues that Lilly's doctrine of equivalents infringement claim is foreclosed by prosecution history estoppel and the disclosure dedication rule. The Court will address each of these threshold arguments in turn.

1. Prosecution History Estoppel

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

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

> cases the patentee can overcome the presumption that prosecution history estoppel bars finding an equivalence.

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

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

On this issue, in the Dr. Reddy's Case, the Court relied on *Regents of University of Cal. v.*

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

Lilly also cites another line of cases that demonstrate that "the tangentiality exception has routinely been applied in cases where the issued claims have been narrowed in a manner that excludes the accused equivalent." (Filing No. 79 at 26.) *See Insituform Technologies, Inc., v. CAT Contracting, Inc.*, 385 F.3d 1360 (Fed. Cir. 2004); *Pfizer Inc., v. Teva Pharmaceuticals U.S.A., Inc.*, 882 F. Supp. 2d 643 (D. Del. 2012). Lilly's amendment focused on distinguishing pemetrexed (the active antifolate) as opposed to methotrexate (a different antifolate) in that the '209

patent was drafted to protect a method of reducing toxicity associated with the administration of pemetrexed disodium. (Filing No. 79 at 28-29). A POSA would regard the salt form of the antifolate (pemetrexed) as peripheral to the amendment. *Id.* at 29. Because the tangentiality exception applies, an independent and dispositive basis under *Festo*, Lilly is not estopped from pursuing infringement under the doctrine of equivalents. The Court need not discuss Hospira's remaining arguments regarding the other two *Festo* exceptions (the foreseeability of tromethamine or that Lilly could have drafted the '209 Patent to claim pemetrexed ditromethamine).

2. Disclosure Dedication Doctrine

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

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

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

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

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

Id. (citations omitted). It is undisputed that pemetrexed ditromethamine was not disclosed specifically in the '209 Patent, rather Hospira's disclosure-dedication argument hinges on Lilly's disclosure of "any antifolate". (Filing No. 74-1 at 35.) Additionally, Lilly asserts that

pemetrexed ditromethamine is not an alternative to pemetrexed disodium, rather the two are the same antifolates because the active moiety—pemetrexed—targets the same relevant enzymes as defined in the '209 Patent specification and understood by a POSA. (Filing No. 79 at 32-33.) Because pemetrexed ditromethamine was not disclosed and identified with specificity, the disclosure-dedication rule does not prevent Lilly from pursuing a doctrine of equivalents infringement theory nor dedicated it to the public.

C. Inducement and Contribution to Infringement

Direct infringement occurs when one party makes, uses, offers to sell, sells, or imports each element of a patented invention. 35 U.S.C. § 271(a). Additionally, a party can be held liable for indirect infringement by actively inducing or contributing to direct infringement by others. 35 U.S.C. § 271(b), (c). "Inducement requires that the alleged infringer knowingly induced infringement and possessed a specific intent to encourage another's infringement." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1056 (Fed. Cir. 2010). Courts have inferred intent to induce infringement based on the contents of labels. *Id.* (holding circumstantial evidence may suffice to prove specific intent to induce infringement). "The pertinent question is whether the proposed label instructs users to perform the patented method. If so, the proposed label may provide evidence of [] affirmative intent to induce infringement." *AstraZeneca*, 633 F.3d at 1060. Similarly, labels may also form the basis to infer intent under contributory infringement when they instruct users to perform a patented method. *See Eli Lilly & Co.*

v. Actavis Elizabeth LLC, 435 Fed.Appx. 917, 926 (Fed. Cir. 2011). In a Hatch-Waxman case such as this, infringement "is focused on the product that is likely to be sold following FDA approval," including the relevant knowledge of the parties at the time the product is sold. *See Abbott Laboratories v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002) ("This determination is based on consideration of all the relevant evidence, including the ANDA filing, other materials submitted by the accused infringer to the FDA, and other evidence provided by the parties.").

Hospira concedes that its label directs the use of folic acid and vitamin B_{12} as set forth in the '209 Patent claims. (Filing No. 79-3 at 16.) Additionally, Hospira also concedes that should this Court find literal infringement of "pemetrexed disodium" or finds that there is no bar to infringement under the doctrine of equivalents, then, as a matter of law, use (and sale) of Hospira's NDA products according to their labeling, would satisfy indirect infringement under both inducement and contributory theories. Moreover, Hospira has not addressed indirect infringement in its summary judgment brief. Because the Court has found Hospira's product literally infringes and that there is no bar to infringement under the doctrine of equivalents, summary judgment is **granted** to Lilly as to Hospira's inducement of and contribution to infringement of the '209 Patent.

IV. CONCLUSION

For the foregoing reasons, Hospira's Motion for Summary Judgment of Non-Infringement (Filing No. 73) is **DENIED** and Lilly's Cross-Motion for Summary

Judgment of Infringement pursuant to literal infringement and doctrine of equivalents (Filing No. 78) is **GRANTED**.

SO ORDERED.

Date: 6/15/2018

/s/ Tanya Walton Pratt
TANYA WALTON PRATT, JUDGE
United States District Court
Southern District of Indiana

Appendix C

United States Court of Appeals for the Federal Circuit

ELI LILLY AND COMPANY,
Plaintiff-Appellee

v.

HOSPIRA, INC.,
Defendant-Appellant

2018-2126, 2018-2127

Appeals from the United States District Court for the Southern District of Indiana in No. 1:16-cv-03460-TWP-MPB, Judge Tanya Walton Pratt.

ON PETITION FOR REHEARING EN BANC

Before PROST, *Chief Judge*, NEWMAN, LOURIE, DYK, MOORE, O'MALLEY, REYNA, WALLACH, TARANTO, CHEN, HUGHES, and STOLL, *Circuit Judges*.

PER CURIAM.

ORDER

Appellant Hospira, Inc. 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

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court