No. 2018-2128

United States Court of Appeals for the Federal Circuit

ELI LILLY & CO.,
Plaintiff-Appellee,

v.

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

Appeal from the U.S. District Court for the Southern District of Indiana, No. 1:16-cv-00308-TWP, Judge Tanya W. Pratt

REPLY BRIEF

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INTRODUCTION

The decision below allows patentees to use the doctrine of equivalents to leverage discrete patent claims that were specifically narrowed during prosecution into a broad evergreening enterprise for their products, turning the tangential exception into a free pass for patentees with prosecution remorse. Lilly's '209 patent emerged from prosecution with narrow claims only to "pemetrexed disodium," having disclaimed all other antifolates. Once Lilly's broader, earlier-issued "pemetrexed" patents expired, Lilly's competitors were entitled to design around the '209 patent's narrower claims. As the opening brief explains, the district court's contrary ruling depends on fundamental departures from precedent concerning the tangential exception, the disclosure-dedication rule, and the test for equivalence.

Any one of the district court's errors independently requires reversal, but the most startling is its treatment of the "tangential" exception to prosecution history estoppel, which is contrary to binding precedent. The Supreme Court has emphasized prosecution history estoppel's importance as a limiting principle to ensure that the doctrine of equivalents does not undermine public notice. This Court has

described the "tangential" exception as "very narrow," and has repeatedly rejected remorse-driven attempts by patentees to walk back narrowing amendments they made in prosecution. Yet, contrary to *Festo*, *Lucent, Integrated Technologies*, *Schwarz*, *International Rectifier, Biagro*, and *Honeywell*, the district court applied the tangential exception—at Lilly's invitation—in a way this Court has never condoned.

Lilly spends most of its brief dodging inconvenient precedent. It describes no fewer than five of this Court's cases rejecting "tangential" arguments similar to Lilly's as "fact-bound," and relies on a clear misreading of *Regents*. Lilly ultimately has no principled defense of the decision below. An affirmance would expand the very narrow tangential exception and undermine the general rule of prosecution history estoppel.

Separately, the district court erred in its treatment of the disclosure-dedication rule and its equivalence analysis. Lilly dismisses contrary disclosure-dedication decisions as unstated "exception[s]" to the fictitious incorporation-by-reference rule applied below, and treats *Warner-Jenkinson*'s reference to "context" as a license to disregard claim language. If precedent is to be faithfully applied rather than disingenuously distinguished, the judgment must be reversed.

ARGUMENT

I. The Tangential Exception Does Not Apply.

All agree that **(1)** Lilly narrowed its claims from "antifolate" to "pemetrexed disodium" for patentability reasons, **(2)** Lilly cannot invoke the doctrine of equivalents for the "pemetrexed disodium" element unless it shows that one of three *Festo* exceptions applies, and **(3)** neither the foreseeability nor "some other reason" exceptions apply. RedBr.21; Appx34. The only question—which this Court considers *de novo*—is whether the "tangential" exception applies. Under binding precedent, it cannot.

A. Lilly Misstates the Legal Standard.

Lilly's main argument relies on a false distinction between why it made the narrowing amendment it did, and why it did not make a different amendment that would have literally covered pemetrexed ditromethamine. RedBr.§I.B. According to Lilly, only "the *reason* that Lilly made the amendment it *actually made*" matters. RedBr.43.

The argument is an empty debater's point. When asking *why* someone made a choice, it is surely relevant to consider what other options were available. Indeed, the Supreme Court describes the prosecution history estoppel exceptions that way. To rebut the

presumption of estoppel, *Festo* explains, "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*." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 741 (2002)[1]; *see Biagro W. Sales, Inc. v. Grow More, Inc.*, 423 F.3d 1296, 1305 (Fed. Cir. 2005); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1312 (Fed. Cir. 2006). The patentee need not rebut all "other hypothetical amendments that it might have considered or that an accused infringer can concoct," RedBr.43-44, but must nonetheless explain why (objectively speaking) it chose the amendment it did rather than one "that would have literally encompassed the alleged equivalent." *Festo*, 535 U.S. at 741.

Consistent with *Festo*, this Court's tangential-exception decisions routinely consider options the applicant had when it amended. Lilly contends that "DRL and Actavis fail to cite a single case in which any court has undertaken such an analysis." RedBr.44. Dr. Reddy's (and Actavis) cited at least two. *Amgen* rejected tangential-exception

[1] *Festo* similarly describes the third exception as "some *other* reason" "the patentee could not reasonably be expected to have described the insubstantial substitute in question." 535 U.S. at 740-41.

arguments like Lilly's, explicitly because the patentee could have drafted an amendment covering the accused equivalent but did not:

> [I]f the patentee had wished only to limit the claims to human EPO, *the patentee could have done so* by continuing to use the adjective "human" when referring to EPO in the third preliminary amendment; *instead the patentee chose to further narrow the claims … by making reference to the specific sequence in Figure 6 rather than human EPO. We thus hold* that Amgen has not met its burden of showing that the … amendment was tangential...

457 F.3d at 1315.

Felix v. American Honda Motor Co., 562 F.3d 1167 (Fed. Cir. 2009), likewise reasoned that if the patentee "had intended *only* to add a channel and not add a gasket, he could easily have simply amended original claim 1 to add [the equivalent] limitation … and not [the gasket] limitation." *Id.* at 1184 (original emphasis). Lilly does not acknowledge that reasoning from *Amgen* or *Felix*. Nor does Lilly cite any case (other than the decision below) refusing to consider whether the patentee could have literally claimed the accused equivalent.

Lilly concedes "tangentiality is a *way* in which a patentee can show that it 'could not reasonably be expected' to have drafted a claim encompassing the equivalent," RedBr.46 (original emphasis), but nonetheless insists that courts cannot consider what claims

encompassing the equivalent the patentee could have drafted. *Id.* at 45-46. Like the district court, Lilly contends that such consideration "collapses the tangentiality exception" with the "separate" unforeseeability exception. *Id.* at 45-47; Appx12. Nonsense. *Festo* explained that the three exceptions derive from common principles and have common characteristics—which include consideration of whether a patentee could have literally claimed the accused equivalent. To point out commonalities does not "collapse" the exceptions any more than it "collapses" cats and dogs to note that both are mammals or house-pets.

Lilly has no explanation for why it could not have drafted claims literally covering pemetrexed ditromethamine.[2] It could have, and in prosecution of its European counterpart application it did. BlueBr.15-17. Lilly cannot distinguish *Amgen, Felix*, or other cases where this Court rejected tangential-exception arguments where the patentee could have drafted a claim covering the accused equivalent but simply chose not to.

[2] The explanation Lilly suggested below hardly helps its cause. Appx2474-2475 n.6. If Lilly claimed pemetrexed disodium because a broader claim would have been invalid under §112, that favors estoppel. *Festo*, 344 F.3d at 1366. The doctrine of equivalents accommodates "language's inability to capture the essence of innovation," *Festo*, 535 U.S. at 734, not an applicant's inability to comply with the Patent Act.

B. The Prosecution Record Cannot Support the Tangential Exception.

1. The Tangential Exception Does Not Excuse Narrowing More Than Absolutely Necessary to Avoid Prior Art.

The *Festo* exceptions are ways to "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*." 535 U.S. at 741. If an applicant *could have* literally encompassed the alleged equivalent but did not because it chose to give prior art a wide berth rather than a narrow one, that showing is not met. This Court has consistently rejected tangential-exception arguments from patentees who simply surrendered more than they needed to. *Integrated Tech. Corp. v. Rudolph Techs., Inc.*, 734 F.3d 1352, 1358 (Fed. Cir. 2013) ("It may be that ITC did not need to surrender a lack of physical contact … to overcome Sato. The dispositive fact is that ITC chose to do so."); *Int'l Rectifier Corp. v. IXYS Corp.*, 515 F.3d 1353, 1359 (Fed. Cir. 2008) ("IR's decision to claim that structure using the limiting term 'adjoining,' whether or not *required* to overcome the rejection, cannot be described as only tangentially related") (original emphasis); *Lucent Techs., Inc. v. Gateway, Inc.*, 525 F.3d 1200, 1217-18 (Fed. Cir.

2008); *Schwarz Pharma, Inc. v. Paddock Labs., Inc.*, 504 F.3d 1371, 1377 (Fed. Cir. 2007). *Festo* and public-notice principles compel that result. *Festo*, 535 U.S. at 731; *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 28-29 (1997); *Schriber-Schroth Co. v. Cleveland Trust Co.*, 311 U.S. 211, 220-21 (1940).

a. Lilly Cannot Distinguish Binding Precedent.

Lilly argues that the "focus" of the tangential-exception inquiry must be "on the *reason* for the amendment, *not the scope of what was surrendered*." RedBr.37. Not so. When considering *why* a patentee made a choice, the other available options are plainly relevant. Otherwise, contrary to *Festo* and this Court's precedent, patentees could avoid estoppel by saying surrendering the alleged equivalent was unnecessary (and thus "tangential") to distinguish prior art.

Festo's directive to consider whether the patentee *could* reasonably have been expected to claim the alleged equivalent necessarily requires consideration of the scope of surrender. 535 U.S. at 741. This Court has considered the scope of surrender when evaluating tangential-exception arguments (*e.g.*, *Integrated Technology, International Rectifier, Lucent,* and *Schwarz*). Lilly dismisses those precedents as "fact-bound,"

RedBr.37 n.5, 40, 47; *id.* at 36 ("facts of the case"), 41 ("different facts"), 42-43, 49 (similar), but never explains how they differ from here. Indeed, Lilly's description of *International Rectifier* matches this case if one merely substitutes "pemetrexed disodium" for "'adjoining' structures." RedBr.37 n.5.

Lilly contends *Regents of the University of California v. Dakocytomation California Inc.*, 517 F.3d 1364 (Fed. Cir. 2008), and *Insituform Technologies, Inc. v. Cat Contracting, Inc.*, 385 F.3d 1360 (Fed. Cir. 2004), support its argument against focusing on "the scope of what was surrendered." RedBr.37. The district court similarly misread *Regents*. Appx35-37. Neither decision supports Lilly; both focused on the substance of the narrowing amendments.

In *Regents*, the relevant patent claimed a method of selectively staining DNA. 517 F.3d at 1377. Before amendment, the claims recited two steps: providing a mixture of "labeled *nucleic acid* fragments" and "disabling the hybridization capacity of repetitive sequences within" that mixture. *Id.* The "disabling" step included "blocking, selective removal, and screening" techniques. *Id.* at 1369. The parties stipulated "nucleic

acid" meant human DNA/RNA, not synthetic nucleic acids like PNA (the accused equivalent). *Id.* at 1376.

In response to a rejection focused on the "disabling" step, the patentee amended its claims to recite the use of "blocking nucleic acid." *Id.* at 1377. But the patentee did *not* amend the "nucleic acid" term *already in the claims*: "the 'nucleic acid' limitation was never narrowed during prosecution and it was not at issue in the office action rejecting the claims, the Examiner Interview Summary Record, or the patentees' remarks accompanying the amendment." *Id.* at 1378. *Regents* thus concluded that prosecution history estoppel did not foreclose the patentee's assertion of PNA as an equivalent to the claimed DNA/RNA "nucleic acid."

The *Regents* amendment differs from Lilly's. Lilly's relevant pre-amendment claim term is "antifolate," which it narrowed to "pemetrexed disodium." *Regents*' relevant term is "nucleic acid," which was not narrowed. Lilly contends the "'nucleic acid' previously recited in the independent claim" in *Regents* was "differ[ent] from the 'blocking nucleic acid' added by the narrowing amendment." RedBr.28-29. It was not. In

Regents, all understood "nucleic acid" to mean the same thing across limitations, both before and after amendment. *Regents*, 517 F.3d at 1378.

Lilly is also wrong to contend that in "*Regents* and here, the reason for the amendment dealt with the first aspect" of the term added by amendment: "'blocking' as opposed to other means of disabling hybridization in *Regents*, and pemetrexed as opposed to another active antifolate (methotrexate) here." RedBr.30. In *Regents*, the patentee's rationale concerned "blocking" precisely because *the "nucleic acid" term was never narrowed*. By contrast, the "antifolate" term undisputedly *was narrowed* during prosecution—*not* to "pemetrexed" as Lilly describes it, RedBr.30 (nor to "pemetrexed and its pharmaceutically acceptable salts" or "a solution comprising pemetrexed," any of which Lilly could easily have said), but to "pemetrexed *disodium*." Lilly exclusively focused on "pemetrexed *disodium*" in its amending remarks. *See infra* pp.12-16.

Insituform likewise considered the substance of the narrowing amendment. There, "'the only *express limitation* put on the invention by Insituform was the use of a vacuum source close to the resin.'" 385 F.3d at 1369-70. Here, the "express limitation" Lilly introduced to distinguish Arsenyan was "pemetrexed disodium."

Lilly's argument, to ignore the substance of the patentee's narrowing amendment in favor of its post-hoc rationalization, founders on precedent and logic. Once the substance of Lilly's amendment is considered, Lilly's arguments fit neatly into a category of tangential-exception arguments this Court has consistently rejected: Lilly narrowed its claims to avoid prior art, and now contends that it surrendered more than it needed to.

b. The Prosecution Record Refutes Lilly's Explanations.

The prosecution record is straightforward, and Lilly tellingly quotes little of it. RedBr.8-9; RedBr.24-25. The relevant document is Lilly's Reply to an Office Action (Appx7874-7884), where Lilly narrowed its claims and explained its reasons.

Lilly narrowed three terms: "antifolate" (to "pemetrexed disodium") "mammal" (to "human") and "methylmalonic acid lowering agent" ("selected from vitamin B12 or a pharmaceutical derivative thereof"):

> 2. (Currently Amended) A method of reducing the toxicity associated with the administration of ~~an antifolate~~ pemetrexed disodium to a ~~mammal~~ human comprising administering to said ~~mammal~~ human an effective amount of ~~said antifolate~~ pemetrexed disodium in combination with a methylmalonic acid lowering agent, selected from vitamin B12 or a pharmaceutical derivative thereof.

Appx7877 (original underlining and strikethrough, highlighting added); BlueBr.14-15. Lilly then asked the examiner to withdraw a rejection for anticipation by Arsenyan:

> Prior Art Rejection Under 35 U.S.C. 102(b)
>
> Claims … are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Arsenyan et al. There is no disclosure in Arsenyan et al. of the invention *as presently claimed*. *In particular*, Arsenyan et al. *does not disclose pemetrexed disodium*
>
> ***and*** *does not disclose* the use of vitamin B_{12} or a pharmaceutical derivative to reduce the toxicity associated with the administration of pemetrexed disodium, or for that matter any other antifolate per the following discussion.
>
> In *view of the present amendments* and the comments above, Applicants respectfully request withdrawal of this rejection.

Appx7880 (paragraph breaks added).

The reason for Lilly's amendment is plain from the record: to narrow its claims and overcome anticipation. Arsenyan's methotrexate disclosure anticipated Lilly's "*antifolate*" claims, so Lilly specifically narrowed them to "*pemetrexed disodium*." Thus, Lilly stated: "There is no disclosure in Arsenyan et al. of the invention *as presently claimed.* In particular, *Arsenyan et al. does not disclose pemetrexed disodium*…." Appx7880. There is no dispute that Lilly deliberately narrowed "antifolate" to "pemetrexed disodium" to avoid prior art. RedBr.8 ("the

purpose of its amendment was to avoid the Arsenyan reference"); RedBr.24 (similar); Appx34. It therefore follows that the tangential exception does not apply. Here, as in *Integrated Technology* and other "I surrendered more than necessary" cases, the patentee's "representations convey to the public that it was relying on [the amended term] *to overcome the prior art.* The public is entitled to rely on those representations." 734 F.3d at 1359.

Lilly nonetheless argues that its amendment was really about "active antifolate pemetrexed," and "pemetrexed disodium" is just a salt form or a variation of that "active antifolate." RedBr.17, 24-26, 28, 30-33, 42. To invoke the "tangential" exception, Lilly was required to show "an objectively apparent reason" for its narrowing amendment, "discernible from the prosecution history record." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1369 (Fed. Cir. 2003) (en banc); *see Pioneer Magnetics, Inc. v. Micro Linear Corp.*, 330 F.3d 1352, 1356 (Fed. Cir. 2003). The prosecution record refutes Lilly's argument.

The difference between what Lilly argues and what it quotes is telling. According to Lilly:

> Lilly explained at the time that the purpose of its amendment was to avoid the Arsenyan reference and its use of methotrexate *by specifying a particular (and different) active antifolate pemetrexed:* "In particular, Arsenyan et al. *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*." Appx7880.

RedBr.8-9. Lilly avoided prior art by claiming only "pemetrexed disodium," Appx7877, and it argued to the examiner in those terms: "*pemetrexed disodium*," not, as Lilly would now have it, "active antifolate pemetrexed." Appx7880-7884. Even the sentence Lilly quotes belies Lilly's argument—it refers *twice*, and *only*, to "pemetrexed disodium." RedBr.8-9 (quoting Appx7880).

Lilly's brief tries to recast its references in prosecution to "pemetrexed disodium" as references to a salt form of "active antifolate pemetrexed." RedBr.8-9. That is not what it said during prosecution, emphasizing instead that the "antifolate" it claimed *was "pemetrexed disodium." See, e.g.*, Appx7880 ("pemetrexed disodium, or for that matter *any other antifolate*"); Appx7883 ("antifolates, *especially pemetrexed disodium*"). In responding to the Arsenyan rejection, and in the referenced "following discussion," Appx7880, Lilly specifically references "pemetrexed disodium"—and only that—*sixteen times* to distinguish

prior art. Appx7880-7884. Each time, Lilly was clear: Lilly previously claimed all "antifolates" but now claimed only one antifolate: "pemetrexed disodium." Not once did Lilly refer to "pemetrexed," "active antifolate pemetrexed," "active moiety," "pemetrexed ion," or any of the similar terms now laced throughout Lilly's brief. Appx7880-7884.

At bottom, Lilly's arguments are not grounded in the prosecution history. They are a strained attempt to avoid stating outright that Lilly's argument is the legal non-starter that it surrendered more than it needed to avoid Arsenyan. This is especially clear in Lilly's repeated assertion that the salt form was "irrelevant" to distinguishing Arsenyan. RedBr.26. In Lilly's view, it could have amended its claims to recite "pemetrexed" or "pemetrexed salts," and the arguments it made in prosecution to distinguish its "pemetrexed disodium" claims from Arsenyan might equally apply to those broader terms. Again that is not what Lilly did, and this Court's precedent—particularly *Integrated Technology*, *International Rectifier*, *Lucent*, and *Schwarz*—holds that what Lilly actually did matters. Lilly may have surrendered more than it needed to, but that does not make Lilly's reasons "tangential."

Lilly similarly latches onto its statement in prosecution that Arsenyan "does not disclose the use of vitamin B12 or a pharmaceutical derivative *to reduce the toxicity associated with the administration of pemetrexed disodium*." RedBr.8-9 (quoting Appx7880); RedBr.25 (same). Lilly contends that, because of how pemetrexed disodium treatment works, "'the 'toxicity associated with the administration of pemetrexed disodium' is the toxicity of pemetrexed itself, rather than of any particular salt form." RedBr.25.

There are three main problems with that argument. *First*, Lilly did not develop it below. Lilly discussed toxicity in connection with *equivalence*, but did not contend for tangential-exception purposes that "'the toxicity associated with the administration of pemetrexed disodium' is the toxicity of pemetrexed itself" outside a solitary paragraph in a reply expert report (Appx8505 ¶60)—certainly not at trial or in summary judgment briefing. Lilly's record citations relate to equivalence. *Compare* RedBr.9-10, 24-25, *with* Appx4391(79:12-16); Appx8403-8405; Appx8504-8507.

Second, the "toxicity" reference in prosecution concerns a *different* amendment Lilly made at the same time. Lilly added "selected from

vitamin B12 or a pharmaceutical derivative thereof" to narrow "methylmalonic acid inhibitor." *See, e.g.*, Appx7877.[3] Having introduced "vitamin B12" into the claims, Lilly relied on that term to distinguish Arsenyan and other prior art. *See, e.g.*, Appx7880 (Arsenyan "does not disclose the use of vitamin B12 … to reduce the toxicity associated with the administration of pemetrexed disodium, or for that matter any other antifolate"); Appx7884 ("None of these references teach the use of vitamin B12 to reduce toxicities associated with an antifolate…"); Appx7882 (John makes "no mention or suggestion of vitamin supplementation…").

Third, Lilly's "toxicity" argument is just another way of saying that Lilly surrendered more than it needed to. The "toxicities which are associated with the administration of pemetrexed *disodium*" may be the same toxicities associated with other pemetrexed salts.[4] Regardless, Lilly did not *claim* other pemetrexed salts, nor did it argue in prosecution

[3] Lilly also added "Vitamin B12" to the patent's title. Appx7876. Such amendments are relevant. *Compare Ruckus Wireless, Inc. v. Innovative Wireless Sols., LLC*, 824 F.3d 999, 1003 & n.2 (Fed. Cir. 2016), *with* RedBr.8 n.3.

[4] Or they may not—Lilly refers in prosecution to "a variety of toxicities," including "at least 23 observed toxicities" "associated with the administration of pemetrexed disodium to patients with advanced colorectal carcinoma." Appx7882.

about other pemetrexed salts. Its claims and arguments referred consistently, exclusively, to "pemetrexed disodium." Appx7880-7884. Lilly may regret those choices, but precedent holds that remorse is not a basis for the tangential exception.

2. The Tangential Exception Does Not Apply Because the Alleged Equivalent and the Reason for Lilly's Amendment Concern the Same Element.

Lilly agrees that the alleged equivalent and the reason for Lilly's amendment concern the same claim element: the "pemetrexed disodium" term. RedBr.47-50. Lilly emphasizes in the companion appeal that "pemetrexed disodium" is one term, not two. Fed.Cir.18-2126, RedBr. at 61 (ECF#28, filed Nov. 13, 2018). *Biagro* and *Honeywell* foreclose Lilly's reliance on the tangential exception. *Biagro*, 423 F.3d at 1306 (rejecting tangential-exception argument "*[b]ecause* both the reason for the amendment and the asserted equivalent relate to the concentration of the fertilizer"); *Honeywell Int'l, Inc. v. Hamilton Sundstrand Corp.*, 523 F.3d 1304, 1316 (Fed. Cir. 2008) ("*Because* the alleged equivalent focuses on the IGV limitation, the amendment bore a direct, not merely tangential, relation to the equivalent.").

Lilly tries to dismiss *Biagro* and *Honeywell* as "fact-bound," and disputes whether those cases "announced a rule." RedBr.47. Regardless of how Lilly labels those cases, they are precedents of this Court that reject arguments indistinguishable from Lilly's. Each decision's reasoning is clear: "because" the reason for the amendment and the accused equivalent related to the same element, the reason was not tangential to the accused equivalent. *Biagro*, 423 F.3d at 1305-06; *Honeywell*, 523 F.3d at 1316. Indeed, in *Honeywell*, that reasoning drew a dissent. 523 F.3d at 1322 (presumption of prosecution history estoppel did "not become irrebuttable simply [because] the accused equivalent concerns the same element that was added by amendment") (Newman, J., dissenting).

Lilly contends *Regents* holds otherwise. RedBr.47, 49. As discussed above, Lilly misreads *Regents*, pp.9-11, *supra*. Indeed, *Regents* confirms the principle applied in *Biagro* and *Honeywell*. In *Regents*, the accused *equivalent* (a synthetic peptide nucleic acid (PNA)) concerned the "nucleic acid" limitation, which literally required human DNA/RNA. 517 F.3d at 1376. The relevant *amendment* (to "blocking nucleic acid") concerned a different limitation (the "disabling …" step). *Id.* at 1377-78. Consistent

with *Biagro* and *Honeywell*, *Regents* relied specifically on the fact that "the 'nucleic acid' limitation was never narrowed during prosecution." *Id.* at 1378. Here, by contrast, the pre-amendment claim term is "antifolate," which was narrowed during prosecution to "pemetrexed disodium" and is the same element for which Lilly wants to rely on the doctrine of equivalents.

Other cases applying the tangential exception likewise turn on the fact that the equivalent and reason for amendment concern *different* elements. *Funai Elec. Co. v. Daewoo Elecs. Corp.*, 616 F.3d 1357, 1369-70 (Fed. Cir. 2010); *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1291-92 (Fed. Cir. 2010). Lilly may view those cases as "fact-bound" too, but they confirm that the district court's ruling expands the tangential exception. Here, like *Biagro* and *Honeywell*, and unlike *Regents* and *Funai*, the purported equivalent and the reason for the amendment concern the same element. If those precedents are applied faithfully, Lilly cannot rely on the tangential exception.

3. An Affirmance Would Expand the "Very Narrow" Tangential Exception and Undermine Prosecution History Estoppel.

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)); *Honeywell*, 523 F.3d at 1315. And rightly so. It is an exception to an exception (prosecution history estoppel) to an exception (doctrine of equivalents) to the principle that a claim's literal terms define the invention (35 U.S.C. §112) and provide notice of the patentee's rights.

Precedent emphasizes the critical importance of prosecution history estoppel in preventing the doctrine of equivalents from undermining public notice. *Warner-Jenkinson*, 520 U.S. at 29 ("[T]he doctrine of equivalents, when applied broadly, conflicts with the definitional and public-notice functions of the statutory claiming requirement."); *Festo*, 535 U.S. at 734 ("Prosecution history estoppel ensures that the doctrine of equivalents remains tied to its underlying purpose."); *Schriber-Schroth*, 311 U.S. at 221 ("The injurious consequences to the public … if patentees were thus permitted to revive cancelled or rejected claims and restore them to their patents are manifest."); *Festo*, 344 F.3d at 1369-70.

In narrow circumstances—as in *Regents* or *Insituform*, where the relevant element was not actually narrowed during prosecution—the tangential exception may relieve patentees from prosecution history estoppel without undermining public notice. But as recognized in *Lucent, Integrated Technologies*, *Schwarz*, *International Rectifier, Biagro*, and *Honeywell*, no legitimate purpose is served—and public notice is undermined—when patentees use the doctrine of equivalents to back out of choices they made in prosecution. As Lilly's brief demonstrates in repeatedly calling those cases "fact-bound," an affirmance here would undermine those precedents by limiting them to their facts and endorsing a rule that courts should ignore what other amendments the patentee might have made.

In prosecution, Lilly focused on the "antifolate" element and declared—to the PTO and the public—that it claimed only "pemetrexed disodium." Appx7877. If there was any doubt about what Lilly claimed or how it distinguished the prior art, it repeated "pemetrexed disodium" *sixteen times* in responding to the examiner's rejections. This is not a case where Lilly "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 could have, but it affirmatively chose instead to claim only "pemetrexed disodium"—relying on that sixteen times. If public notice means anything, it means that Lilly, not the public, should bear the consequences of that clear, repeated, emphatic choice. The district court's contrary judgment must be reversed.

II. The Disclosure-Dedication Rule Requires Reversal.

Like prosecution history estoppel, the disclosure-dedication rule is an important, independent limit on the doctrine of equivalents, *Johnson & Johnston Assocs. Inc. v. R.E. Serv. Co.*, 285 F.3d 1046, 1054-55 (Fed. Cir. 2002) (en banc), and an issue this Court reviews without deference. RedBr.21. This Court's precedent holds that **(1)** the disclosure-dedication rule does not limit a patent's "disclosure" to the text of the specification plus what it incorporates by reference, **(2)** the disclosure-dedication rule does not impose a §112 test, and **(3)** an external document like Akimoto, that the patent-in-suit references, should be read together with the patent-in-suit rather than in isolation. At Lilly's invitation, the district court ran afoul of all three principles. On appeal, Lilly repeats the district court's erroneous reasoning.

1. The district court erroneously believed that "the disclosure-dedication rule does not bar Lilly's doctrine of equivalents claim," "*[b]ecause* Akimoto was not expressly incorporated, *as required*, in the '209 patent." Appx14. Lilly doubles down in arguing for an incorporation-by-reference rule, contending Akimoto is "[u]nincorporated," RedBr.54, and that "[n]othing in [the '209 patent] adopts everything said in these references as part of the '209 patent." RedBr.53. Lilly cites *Toro Co. v. White Consolidated Industries, Inc.*, 383 F.3d 1326 (Fed. Cir. 2004), *PSC Computer Products, Inc. v. Foxconn International, Inc.*, 355 F.3d 1353 (Fed. Cir. 2004), and *Johnson*, but none of those cases even addressed references outside the patent, incorporated or otherwise.

Lilly also relies on *SanDisk Corp. v. Kingston Technology Co.*, 695 F.3d 1348, 1364 (Fed. Cir. 2012), but *SanDisk* merely holds that incorporation-by-reference *can* satisfy the disclosure-dedication rule. It does not hold that *only* incorporation-by-reference can do so. Lilly's reading of *SanDisk* is wrong, and inconsistent with other decisions that Lilly fails to distinguish. *See* BlueBr.63-65; *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1297 (Fed. Cir. 2009); *CSP Techs., Inc. v. Sud-Chemie AG*, 643 F.

App'x 953, 958 (Fed. Cir. 2016) (addressing *SanDisk* and rejecting Lilly's reading of it).

Lilly acknowledges that *Abbott* and *CSP* applied the disclosure-dedication rule without requiring incorporation-by-reference. RedBr.53; *Abbott*, 566 F.3d at 1297; *CSP*, 643 F. App'x at 958. That should be the end of the matter, but Lilly dismisses those inconvenient precedents as "exceptions." RedBr.53. Not so. Neither *Abbott* nor *CSP* state any rule requiring incorporation-by-reference, nor do they purport to apply any "exception" to a non-existent incorporation-by-reference rule. They apply the disclosure-dedication rule as the district court should have done here.

2. Lilly also fails to defend the district court's erroneous requirement of explicit disclosure of "pemetrexed ditromethamine" as an "alternative" to pemetrexed disodium. The disclosure-dedication rule "does *not* impose a §112 requirement on the disclosed but unclaimed subject matter." *Toro*, 383 F.3d at 1334. The standard is less stringent and requires a "determin[ation] from the specification's disclosure whether 'one of ordinary skill would have come to the conclusion that the inventor[] ha[s] identified [the unclaimed embodiment] as an alternative to [the claimed embodiment]." *CSP*, 643 F. App'x at 959.

Here, the district court applied a standard *more* stringent than §112. Section 112 itself "does not demand … that the specification recite the claimed invention *in haec verba*." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2010) (en banc). The district court nonetheless reasoned that because "Akimoto does not *specifically* disclose *pemetrexed ditromethamine* as an alternative to pemetrexed disodium, the disclosure-dedication rule does not bar Lilly's doctrine of equivalents claim." Appx14. Again, Lilly's answer is to double down. Rather than defending the district court's erroneous rule, Lilly repeats it, contending that "the specification of the '209 patent does not *expressly* disclose 'pemetrexed ditromethamine,'" and that "alone[,] should end the analysis," RedBr.51, and emphasizing that the '209 patent and Akimoto do not "expressly" or "specifically" disclose pemetrexed ditromethamine. RedBr.51, 54, 56, 58. No precedent supports the explicit-disclosure-as-an-alternative rule the district court applied, and *Toro* and *CSP* reject it.

3. The district court erroneously read Akimoto in isolation, calling it a "generic reference," Appx14, and reasoning that "no POSA would understand Akimoto to specifically disclose pemetrexed, tromethamine, or pemetrexed ditromethamine … unless they knew to go looking for it."

Appx38-39. But the disclosure-dedication doctrine is fundamentally about the *'209 patent's* disclosure to a POSA either directly or by reference to other documents, *CSP*, 643 F. App'x at 959—not Akimoto in isolation. In other words, what the district court misunderstood is that the '209 patent tells the POSA "to go looking for it," based on the specification's discussion of Akimoto.

Lilly agrees a proper analysis considers what a skilled artisan would find in Akimoto with the '209 patent in hand—not in isolation. RedBr.61 (citing BlueBr.59-61). But Lilly's defenses of the district court's reasoning implicitly deny that premise. Lilly thus repeats that pemetrexed and tromethamine are not "expressly disclosed" or "specifically identif[ied]" *in Akimoto*. RedBr.55-56, 58. Perhaps not in isolation, but with the '209 patent in hand, a skilled artisan readily finds pemetrexed ditromethamine disclosed by Akimoto. The '209 patent indicates that Akimoto discloses "[p]referred examples of antifolates" as alternatives to the "most preferred" and only claimed antifolate, "[p]emetrexed [d]isodium." Appx49(4:34-43). Although Lilly points to the need to "select[] the correct values for seven unique variables in the Formula I structure" in Akimoto to arrive at pemetrexed, RedBr.55, Lilly does not

dispute that doing so is a "very straightforward process" a skilled artisan could do "quickly" with the '209 patent in hand. Appx4632-4635(320:25-323:22). And Lilly's expert confirmed Akimoto discloses pemetrexed. Appx4561(249:4-13).[5]

Lilly contends that Akimoto lists "a large and unquantifiable roster of potential salt agents," "of which tromethamine is but one." RedBr.57. Even if true in isolation, that is not the proper analysis: A POSA would read Akimoto with an understanding of the technology and with the '209 patent in hand. Lilly does not contend the number of *pharmaceutically acceptable* salts was unquantifiable. The number was undisputedly small and tromethamine was one of the most common substituted ammonium bases in injectable drugs, including as an alternative for sodium. BlueBr.58-61.

The opening brief noted that "tromethamine in particular was one of a handful of substituted ammonium bases that were FDA-approved."

[5] Lilly disputes whether its expert "conceded that pemetrexed is disclosed in" Akimoto. RedBr.55. He "agree[d] that this disclosure [in Akimoto] includes the compound pemetrexed," and conceded, "this family of compounds contains one of the chemical structures of pemetrexed." Appx4561(249:11-15). Whether Akimoto uses the words "pemetrexed ditromethamine" is not the test.

BlueBr.60-61. Lilly responds that "Akimoto contains no such limit." RedBr.58. But whether Akimoto in isolation "limit[s]" its disclosure to FDA-approved salts is beside the point. *Id.* The '209 patent refutes any suggestion a POSA would view all salts as an undifferentiated mass. The '209 patent lists as "[p]referred examples of antifolates" FDA-approved drugs (e.g., "Methotrexate") *and* "derivatives described by Akimoto." Appx49(4:34-43). Akimoto describes its invention as useful "antineoplastic [anti-tumor] agents," including their "pharmaceutically acceptable" salts. Appx7952-7953. As a matter of law, a skilled artisan with the '209 patent in hand would have understood Akimoto to disclose *at least* FDA-approved substituted ammonium salts of pemetrexed, including pemetrexed ditromethamine. *See Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1362 (Fed. Cir. 2007); *Richardson-Vicks Inc. v. Upjohn Co.*, 122 F.3d 1476, 1477, 1480 (Fed. Cir. 1997); *Allergan Inc. v. Sandoz, Inc.*, 726 F.3d 1286, 1291-92 (Fed. Cir. 2013).

Lilly contends that Dr. Reddy's "effectively" equates the disclosure-dedication standard with obviousness "in light of the specification and the prior art cited therein." RedBr.61. That is a nonsequitur. Precedent holds that the disclosure-dedication standard is less stringent than §112,

Toro, 383 F.3d at 1334, and the §112 standard, in turn, is more stringent than obviousness. *Ariad*, 598 F.3d at 1352. Whether there is any relevant direct comparison between the disclosure-dedication and obviousness standards is not a question the Court needs to answer to resolve this appeal. The disclosure-dedication inquiry is whether, "from the specification's disclosure … 'one of ordinary skill would have come to the conclusion that the inventor[] ha[s] identified [the unclaimed embodiment] as an alternative to [the claimed embodiment]." *CSP*, 643 F. App'x at 959. Rather than applying the proper standard, the district court required incorporation-by-reference and explicit disclosure of "pemetrexed ditromethamine" as an "alternative," and read Akimoto in isolation. Those errors require reversal.

III. The District Court's Equivalence Ruling is Legally Erroneous.

Lilly's claims recite "method[s] *for administering* pemetrexed disodium" to cancer patients. Appx52-53. No claim requires that the pemetrexed disodium have any particular efficacy. The prosecution record reaffirms that Lilly's claims are not directed to how the drug may treat tumors. Lilly began with claims to "method[s] of inhibiting tumor growth," BlueBr.18; Appx6599; Appx6616-6617, but dropped them after

the PTO concluded those claims were not enabled. Appx6674. Lilly thereafter confined its claims to "method[s] for administering." BlueBr.18; Appx52-53.

The district court thus legally erred when it focused its equivalence analysis on a comparison of how pemetrexed ditromethamine and pemetrexed disodium *treat tumors*, and dismissed as "irrelevant" any comparison of how those drugs can be *administered*. Appx17 ("Under the relevant context that *the claim relates to medical treatment*, pemetrexed ditromethamine *treats the patient's cancer* in exactly the same way as pemetrexed disodium."); Appx18 (other differences are "irrelevant"). The equivalence analysis is rooted in claim language, not the invention as a whole, and not a patentee's desire to exclude competition. *Festo*, 535 U.S. at 731-32; *Warner-Jenkinson*, 520 U.S. at 28-29.

Lilly's contrary arguments are unsound.

1. The judgment rests on two claims that depend from claim 1 (9 and 10), and also on claim 12 and seven of claim 12's dependent claims (13-15, 18, 19, 21, and 22). Appx1. Claim 1 is below. The language Lilly emphasizes is underlined.

> **1.** A method for administering pemetrexed disodium to a patient in need thereof comprising administering an effective amount of folic acid and an effective amount of a methylmalonic acid lowering agent followed by administering an effective amount of pemetrexed disodium, wherein
>
> the methylmalonic acid lowering agent is selected from the group consisting of vitamin B12, hydroxycobalamin, cyano-10-chlorocobalamin, aquocobalamin perchlorate, aquo-10-cobalamin perchlorate, azidocobalamin, cobalamin, cyanocobalamin, or chlorocobalamin.

Appx52-53. Lilly emphasizes "to a patient in need," RedBr.65-66, but that means only that the drug is given to a cancer patient, not that the drug must have any effect or achieve any result.

Lilly also emphasizes "an effective amount," RedBr.65, but the parties' agreed-upon construction refutes Lilly's effort to cast claim 1 as a "treatment" claim. The parties agreed that "effective amount of pemetrexed disodium" meant only "an amount of pemetrexed disodium that is *capable of* providing a therapeutic benefit to the patient in need thereof." Appx1169. In other words, *any amount* that *could possibly* benefit a patient is sufficient; it does not matter what, if any, therapeutic effect actually happens.

The other eight claims (claim 12 and its dependent claims) are even worse for Lilly. Claim 12 is below.

> **12.** An improved method for administering pemetrexed disodium to a patient in need of chemotherapeutic treatment, wherein the improvement comprises:
>
> > a) administration of between 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.

Appx53. Claim 12 contains no language requiring or even implying that the administered substances have any effect on the patient. It does not even refer to "effective amount[s]" of pemetrexed disodium. Each step refers to "administration," without specifying any dose of pemetrexed disodium, or requiring any effect.

Lilly again emphasizes the "patient in need" term. RedBr.64-65. But as with claim 1, claim 12 recites administration *to* a cancer patient, not the administered substances must have any effect on the patient. Lilly calls claim 12 "a 'Jepson-style' claim" because of the preamble's "improve[ment]" language. RedBr.67. To the extent relevant, that further supports reversal. A "Jepson" claim's preamble has "structural importance" and "defines not only the context of the claimed invention, but also its scope." *Rowe v. Dror*, 112 F.3d 473, 479 (Fed. Cir. 1997).

Claim 12's preamble recites a "method for *administering*," which underscores the district court's error in analyzing the claims as if they recited "method[s] of treating tumors."

Lilly refers repeatedly to "context," but in substance Lilly is either stretching the "patient in need" language or invoking the truism that pemetrexed disodium is a cancer drug. RedBr.16, 19, 63-69. That latter point cannot bear the weight Lilly places on it. Pharmaceutical patent claims take many forms, and any drug can be the subject of numerous claims of varying scope (*e.g.*, molecules, dosing amounts, dosing forms, methods of treatment, methods of administration). "Equivalence" and "context" are not a license for treating all such claims as interchangeable to allow the patentee to extend its market exclusivity indefinitely. Even under the doctrine of equivalents, claim language matters. *Warner-Jenkinson*, 520 U.S. at 28-29. The language Lilly chose—"method[s] for administering" regardless of efficacy—cannot be reconciled with an equivalence analysis focused on the effect on the patient.

2. Lilly's remaining arguments try to construct an equivalence analysis unmoored from any claim language.

Lilly refers to the "goal" or intended "result" of the claimed methods. RedBr.65 n.8, 66-67. That argument contradicts *Warner-Jenkinson*'s holding that "the doctrine of equivalents must be applied to individual elements of the claim, not to the invention as a whole." 520 U.S. at 29. Where no individual elements recite Lilly's "goal" or "result," an equivalence analysis focused on those things is fundamentally misdirected.

Lilly emphasizes the finding that a POSA is an oncologist. RedBr.16, 67. That only underscores the district court's error. Although the claims are indifferent to whether the drug has any effect, the district court believed it was *required* to focus on treatment outcomes and disregard chemical differences once it decided that the POSA is an oncologist rather than a chemist. The court regarded that finding as "critical (and dispositive)" of equivalence. Appx16; RedBr.16 (quoting *id.*). Lilly has no answer for the point that an oncologist and a chemist would not read the *claims* differently. "Pemetrexed disodium" does not mean one thing to an oncologist and another to a chemist. To hold that a POSA's job description or goals are "critical (and dispositive)" of equivalence, Appx16, ignores the claim language, defies *Warner-*

Jenkinson's holding that "the doctrine of equivalents must be applied to individual elements of the claim," 520 U.S. at 29, and allows the doctrine to "take[] on a life of its own, unbounded by the claims." *Id.* at 28-29.

3. Lilly suggests that the court's error was harmless because, according to Lilly, Dr. Reddy's does not explain how chemical differences between pemetrexed disodium and pemetrexed ditromethamine "are relevant in the context of a liquid administration." RedBr.69.

It was Lilly's burden, not Dr. Reddy's, to prove that chemical differences do not affect administration. *AquaTex Indus., Inc. v. Techniche Sols.*, 479 F.3d 1320, 1328 (Fed. Cir. 2007). The court never weighed evidence on that score because it viewed chemical differences as "irrelevant." Appx18. Lilly contends "it is undisputed that those differences have *no impact* on how pemetrexed ditromethamine and pemetrexed disodium are administered." RedBr.69 (original emphasis) (citing Appx4429-4434; Appx4499-4501; Appx4526-4532; Appx4706-4709). But the testimony Lilly cites says no such thing. Dr. Reddy's expert discusses only buffering capacity (not solubility, stability, pH, or other differences) and never agrees that the different buffering capacities do not affect administration. Appx4706-4709.

Further, the court's statement that the POSA's identity was "critical (and dispositive)" of equivalence confirms that the error was *not* harmless. If the court thought that a focus on chemical differences would produce the same result as the erroneous focus on treatment, it would not have described the oncologist/chemist distinction as "critical (and dispositive)." It would have said the opposite. The error was not harmless.

CONCLUSION

The district court's judgment should be reversed.

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CERTIFICATE OF SERVICE

On January 16, 2019, this brief was submitted to the Court by CM/ECF, and thereby served on all parties.

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CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATION

This brief complies with the type-volume limitations of Fed. R. App. P. 32 and Fed. Cir. R. 32. According to the word-processing system used to prepare it, the brief contains 7,000 words.

/s/ John C. O'Quinn