Nos. 2018-2414, 2019-1086

United States Court of Appeals for the Federal Circuit

AMGEN INC.,
Plaintiff-Appellant,

v.

AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK LLC, PIRAMAL HEALTHCARE UK LIMITED,
Defendants-Appellees,

ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., dba Zydus Cadila,
Defendants-Cross-Appellants.

On appeal from the United States District Court for the District of Delaware, Case No. 1:16-cv-00853-MSG

PETITION OF AMGEN INC. FOR REHEARING AND REHEARING EN BANC

Wendy A. Whiteford
Lois M. Kwasigroch
Eric M. Agovino
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, CA 91320
Telephone: (805) 447-0464

John D. Murnane
Joshua I. Rothman
Alicia A. Russo
VENABLE | FITZPATRICK
Venable LLP, 1290 Avenue of the Americas
New York, NY 10104-3800
Telephone: (212) 218-2100

Bradford J. Badke
Sona De
SIDLEY AUSTIN LLP
787 Seventh Avenue
New York, NY 10019
Telephone: (212) 839-5300

Ryan C. Morris
Joshua J. Fougere
Lauren Cranford Katzeff
SIDLEY AUSTIN LLP
1501 K Street, N.W.
Washington, DC 20005
Telephone: (202) 736-8000

Counsel for Plaintiff-Appellant Amgen Inc.

February 13, 2020

CERTIFICATE OF INTEREST

Counsel for Plaintiff-Appellant Amgen Inc. certifies the following:

1. The full name of every party represented by me is:

Amgen Inc.

2. The names of the real parties in interest represented by me are:

See response to number 1.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the parties represented by me are:

None.

4. The names of all law firms, and the partners or associates, that appeared for the party represented by me in the trial court or are expected to appear in this Court and who are not already listed on the docket for the current case are:

Venable LLP (formerly, Fitzpatrick, Cella, Harper & Scinto)
Frederick C. Millett, Erica L. Norey, Gabrielle Markeson, James R. Tyminski, Robert S. Pickens, Rosanna W. Gan, Kathryn E. Easterling, Una Fan

Morris, Nichols, Arsht & Tunnell LLP
Jack B. Blumenfeld, Maryellen Noreika

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this Court's decision in the pending appeals is:

Counsel for Amgen is aware of one pending consolidated case before this Court that may be directly affected by the decision here: *Amgen Inc. v. Watson Laboratories, Inc.*, No. 2019-1650, docketed March 14, 2019. That appeal concerns the same district court case and the same patent, U.S. Patent No. 9,375,405 (the '405 patent) at issue here.

Counsel for Amgen is unaware of any other related case(s) pending in this or any other court that will directly affect or be affected by the decision on appeal.

/s/ Bradford J. Badke
Bradford J. Badke

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STATEMENT OF COUNSEL

Based on my professional judgment, I believe the panel's decision in this case is contrary to the following decisions of the Supreme Court of the United States and of this Court: *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722 (2002) ("*Festo VIII*"); *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359 (Fed. Cir. 2003) (en banc) ("*Festo IX*"); *Ajinomoto Co. v. ITC*, 932 F.3d 1342, 1355 (Fed. Cir. 2019); *Eli Lilly & Co. v. Hospira, Inc.*, 933 F.3d 1320, 1331 (Fed. Cir. 2019); *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1292 (Fed. Cir. 2010).

Based on my professional judgment, I believe this appeal requires an answer to one or more precedent-setting questions of exceptional importance:

1. Whether, in order to identify the scope of territory surrendered through a prosecution amendment, the Court must identify and address the predicate "rationale underlying the amendment" before it can decide whether the rationale "bears no more than a tangential relation to the equivalent in question."

2. Whether the mere fact that an equivalent appeared in the cited prior art—without more—automatically means that an amendment made during prosecution precludes the equivalent in question.

/s/ Bradford J. Badke
Bradford J. Badke
Counsel of Record for Amgen Inc.

INTRODUCTION

Amgen Inc. respectfully requests panel rehearing or, alternatively, rehearing en banc on a specific but important aspect of the panel's decision: whether the panel overlooked the proper analysis of the scope of surrendered territory to hold that prosecution history estoppel bars Amgen from asserting that Piramal's pregelatinized starch (PGS) is an equivalent binder. Rehearing is necessary to avoid a conflict between the panel's holding, the decision in *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722 (2002) ("*Festo VIII*"), and this Court's decisions applying *Festo VIII*.

This case concerns Amgen's U.S. Patent No. 9,375,405 covering Sensipar®, a first-in-class drug composed of active ingredient cinacalcet hydrochloride and three categories of inactive ingredients (or "excipients"). Elements (a) through (d) of asserted claim 1 cover, respectively, cinacalcet hydrochloride, diluents, binders, and disintegrants. APPX152. The binder and disintegrant limitations contain Markush groups that were added during prosecution.[1] The listed binders are all

[1] Markush groups generally must "possess at least one property in common …, and it is clear from their very nature or from the prior art that all members possess this property." MPEP 706.03(y).

"hardening" binders.[2] *Id.* Piramal makes a copy of Sensipar® that uses PGS as a hardening binder, which is not listed in the binder Markush group.

The panel held that prosecution history estoppel applies. More specifically, after holding that an Examiner's Amendment to add two Markush groups was narrowing and that Amgen had not rebutted the presumption that this was for reasons substantially related to patentability, the panel stated without qualification that "Amgen [thus] surrendered equivalent but unclaimed binders and disintegrants." Slip Op. 24. That "surrender," however, was just a *presumption* according to law, the scope of which required further analysis. *Festo VIII*, 535 U.S. at 740-41. The panel did not address Amgen's contentions that the record shows patentability rested on the "nature" of the claimed excipients (*i.e.*, hardening binders), which achieved a "unique dissolution profile" for a claimed amount of cinacalcet hydrochloride, and that Amgen therefore did not relinquish all binders as equivalents, just those that lacked a hardening nature. *See* ECF No. 54, at 51. Instead, the panel stated only that Piramal's binder appeared in the cited prior art, and that an amendment "made to avoid prior art that contains the equivalent in question is not tangential." Slip Op. 24-25 (quoting *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1291 (Fed. Cir. 2010)).

[2] Binders hold (or bind) the tablet together. Hardening binders work by hardening upon drying after a manufacturing process known as "wet granulation." APPX3328. Not all binders are hardening binders.

That decision overlooked or misapprehended the need to "address[] the scope of the subject matter surrendered," and the need to identify the "objectively apparent reason for the narrowing amendment" in order to determine whether that rationale was "tangential" to the equivalent. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1369-70 (Fed. Cir. 2003) (en banc) ("*Festo IX*"). Taking the required analytical steps in this case, moreover, reveals that Amgen did not surrender all territory between the original and amended claims but surrendered only binders that are *not* hardening binders. It was legal error to allow a presumption to control the outcome here without first addressing the rationale underlying the amendment to determine whether the presumption was overcome based on the tangential exception.

If the panel does not grant rehearing, then the en banc Court should do so. In addition to neglecting the need to assess "the rationale underlying the narrowing amendment," the panel read *Intervet*, 617 F.3d 1282, too broadly. The simple fact that the equivalent in question appears in the prior art does not, contrary to the panel decision, automatically establish that the amendment was "made to avoid [that aspect of the] prior art." Allowing the panel's over-reading of *Intervet* to stand, moreover, risks creating a new and categorical rule of precisely the type that the Supreme Court rejected in *Festo VIII*—a rule that would be particularly

draconian for formulation patents, where the prior art often contains long lists of pharmaceutically acceptable excipients. Rehearing would avoid that result.

BACKGROUND

A. Legal Background

The doctrine of equivalents is "a firmly entrenched part of the settled rights protected by the patent." *Festo VIII*, 535 U.S. at 733. It allows patentees to protect their inventions from the "unscrupulous copyist," *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 607 (1950), particularly since "the nature of language makes it impossible to capture the essence of a thing in a patent application," *Festo VIII*, 535 U.S. at 731.

Prosecution history estoppel places limitations on equivalents, *Eli Lilly & Co. v. Hospira, Inc.*, 933 F.3d 1320, 1330 (Fed. Cir. 2019), but, to maintain patent protection, those limitations are not absolute. In *Festo VIII*, the Supreme Court explicitly rejected the proposition that amendment-based estoppel erects a "complete bar" to equivalents. 535 U.S. at 737. Instead, a narrowing amendment made for reasons of patentability establishes only a "presumption that the patentee has surrendered all territory between the original claim limitation and the amended claim limitation." *Festo IX*, 344 F.3d at 1367. Critically, that presumption "is *not … just [a] complete bar by another name*." *Festo VIII*, 535 U.S. at 741 (emphasis added).

Once a court determines that a narrowing amendment has been made for a substantial reason relating to patentability, the presumption does not end the analysis. Rather, because there will be instances "where the amendment cannot reasonably be viewed as surrendering a particular equivalent," *id.* at 740-41, then "*the [next] question* … addresses the scope of the subject matter surrendered," *Festo IX*, 344 F.3d at 1367 (emphasis added). A patentee can rebut the presumption—and thus narrow the scope of surrender—when, for example, "the rationale underlying the amendment … bear[s] no more than a tangential relation to the equivalent in question." *Festo VIII*, 535 U.S. at 740. As numerous decisions recognize, that inquiry logically has to start by identifying what the "rationale" or "reason" for the amendment is, and then deciding whether the patentee has overcome the presumption of complete surrender. *See, e.g.*, *Ajinomoto Co. v. ITC*, 932 F.3d 1342 (Fed. Cir. 2019); *Eli Lilly*, 933 F.3d 1320; *Intervet*, 617 F.3d 1282.

B. Procedural History

Amgen sued various defendants who sought FDA approval to market generic copies of Sensipar®. APPX3-45. Relevant here, the district court determined that defendant Piramal's product did not infringe because it did not meet the '405 patent's binder limitation. APPX30-38. Because Piramal's product uses PGS as a hardening binder, APPX3687, and because PGS is not listed in element (c), Amgen asserted the doctrine of equivalents. The district court held

that prosecution history estoppel barred Amgen from claiming Piramal's PGS as an equivalent.[3]

A panel of this Court affirmed. Slip Op. 21-25. During prosecution, an Examiner's Amendment had moved two Markush groups—a binder group and a disintegrant group—from then-dependent (and also rejected) claims and added them to elements (c) and (d) of claim 1. *Id.* The excipients listed in the Markush groups of elements (c) and (d) are identified in the specification as exemplary binders and disintegrants. APPX148(6:58-64). The panel held that "Amgen failed to carry its burden to demonstrate that [this] Amendment was made for a reason unrelated to patentability" because, if Amgen were correct, "the Examiner proposed the Examiner's Amendment for no purpose at all." Slip Op. 24.

That holding established only a presumption that Amgen had "surrendered all territory between the original claim limitation and the amended claim limitation," *Festo IX*, 344 F.3d at 1367, but the panel went further. It first stated categorically that "Amgen surrendered equivalent but unclaimed binders and disintegrants," Slip Op. 24—a proposition that the district court declined to adopt, APPX37-38. The panel then failed to consider any argument about the scope of the surrender, and held that (1) the prior art included the claimed equivalent, and

[3] The decision has the illogical effect of surrendering starch from the scope of equivalents to the binder element (c) although it is literally claimed in element (b).

(2) an "amendment made to avoid prior art that contains the equivalent in question is not tangential." Slip Op. 24-25 (quoting *Intervet*, 617 F.3d at 1291).

ARGUMENT

The panel's truncated analysis failed to properly decide surrendered scope and should be corrected either by the panel or through a remand to the district court. If the panel adopts neither of those courses, then the full Court should grant rehearing en banc to cure the existing conflict between well-established precedent and the decision's erroneous bright-line rule about the tangential exception.

I. THE PANEL'S PROSECUTION HISTORY ESTOPPEL DECISION WARRANTS REHEARING.

Even assuming that the Examiner's Amendment was narrowing and for reasons of patentability, Slip Op. 24, the panel "overlooked or misapprehended" the parties' arguments related to the scope of surrender and the legal inquiry required to decide what that scope is. Fed. Cir. R. 40(a). The panel should grant rehearing on that narrow issue.

The parties offered different rationales for the Examiner's Amendment, but both ultimately should have led to the same result about the scope of surrender. Relying on the Examiner's stated reasons for allowance, Amgen argued that the amendment clarified that the point of novelty for the binders was their "nature" as hardening binders. *See, e.g.*, ECF No. 54, at 50-52; Slip Op. 23-24 (reciting

Amgen's argument that the amendment "explained in more explicit terms" the nature of the binders); APPX4488. Here is how the Examiner put it:

> claimed compositions are distinguished from the closest prior art by the amount of cinacalcet HCI, *the nature of the excipients* and their respective amounts.

APPX10193 (emphasis added); *see also* APPX10717; APPX10773. The rationale was therefore *not* the specific identities of the binders listed in element (c), which makes sense because the prior art disclosed all listed binders, and the rationale was *not* the weight limitations, which also makes sense because those were a part of the claims before amendment. Amgen therefore retained binders having the "nature" of the claimed hardening binders and their equivalents, and only surrendered binders of non-hardening nature. By including hardening binders within the scope of surrendered equivalents, the panel's holding was too broad.

Piramal articulated a different "rationale," and the district court adopted it. In their view, the reason for the amendment was that the "smaller set" of binders and disintegrants in the amended claim distinguished the larger number disclosed in the prior art. Slip Op. 23 (articulating Piramal's stated rationale); APPX37 ("the Examiner's Amendment was able to overcome the prior art by claiming a smaller set of the binders disclosed in the prior art"). That rationale is not stated in the prosecution record. But even if true, it is consistent with the prosecution history's statements that patentability rested on the "nature" of the listed hardening binders.

Hardening binders are *by definition* a "smaller set" than all binders recited by the pre-amendment claims. The territory surrendered, in turn, was still at most *non-hardening* binders, because the rationale for the amendment (according to Piramal) was to shrink the universe of binders from all binders shown in the prior art—*which undisputedly included all members of the Markush groups*—to those of a particular "nature." Amgen "did not surrender the ability to claim as equivalents other hardening binders." ECF No. 54, at 52.

The panel "overlooked or misapprehended" the stated rationales for the amendment and thus did not apply the proper legal standard to measure the scope of surrender. After reciting the parties' competing rationales for the amendment, Slip Op. 23, the panel never returned to them, *id.* at 24-25, nor did it otherwise properly consider whether the presumption was overcome and whether the objectively evident rationale for the amendment was or was not tangential to the accused equivalent. *Festo IX*, 344 F.3d at 1367; *Ajinomoto*, 932 F.3d at 1355-56 (noting the court's responsibility to "identif[y] what was not within the 'scope disclaimed'"). Notices of allowance throughout the prosecution made repeated reference to the "nature of the excipients," ECF No. 54, at 53-54, and yet the panel never considered them, Slip Op. 22-25. The Examiner's Amendment was not made to overcome hardening binders in the cited prior art, and its rationale was thus tangential to the PGS equivalent.

Rather than address the disputed rationales provided by the parties, the panel applied a bright-line rule that the tangential exception cannot apply when an amendment is made "to avoid prior art that contains the equivalent in question." Slip Op. 24-25 (quoting *Intervet*, 617 F.3d at 1291). That reasoning effectively erases the tangential exception that the Supreme Court adopted. The panel decision risks setting up a regime where every time an asserted equivalent is mentioned in the prior art then any subsequent amendment will necessarily be "made to avoid" the equivalent, such that the tangential exception is automatically unavailable, and the presumption controls. That cannot be correct, especially when, as here, the recited art included the same excipients in the same amounts as were ultimately claimed and allowed. *See, e.g.*, APPX10914 (disclosing a composition with two listed diluents (mannitol and microcrystalline cellulose), a listed binder (povidone), and a listed disintegrant (sodium starch glycollate) in the claimed weight percentages). The Examiner's Amendment therefore *could not have been* "made to avoid" all prior art binders. Piramal has never been able to persuasively answer that critical flaw in its position. *See, e.g.*, Oral Arg. at 31:28-32:08.

The panel should grant rehearing to conduct the proper scope analysis and either hold that Amgen did not surrender hardening binders, or remand for the district court to consider the scope of surrender anew. At a minimum, moreover,

the panel should clarify that the statement "Amgen surrendered equivalent but unclaimed binders and disintegrants," Slip Op. 24, was merely a recitation of the *Festo VIII* presumption and not a broader holding about the scope of surrender.

II. IF THE PANEL DOES NOT GRANT REHEARING, THEN REHEARING EN BANC IS WARRANTED.

If the panel does not rehear the case, then the full Court should grant rehearing to remedy a conflict with *Festo VIII* and its progeny. Fed. Cir. R. 35(b)(1). The panel decision raises two related and important issues, each of which warrant en banc consideration.

A. The *Festo* Presumption Cannot Control Until the Court Considers Whether the Rationale For Amendment Was Tangential.

The first issue raised by the panel decision relates to the proper analysis under *Festo VIII* in deciding the scope of equivalents surrendered. More specifically, once a "court determines that a narrowing amendment has been made for a substantial reason relating to patentability … then *the [next] question* … addresses the scope of the subject matter surrendered." *Festo IX*, 344 F.3d at 1367 (emphasis added). The panel did not do that, and its failure to address the rationale for the amendment left the analysis incomplete.

Many of this Court's cases recognize that the court must consider whether the amendment was made for a reason unrelated—*tangential*—to the equivalent.

If so, the equivalent is not in the scope of surrender. These cases conflict with the panel decision.

The first is, ironically, the case that the panel cited to reject Amgen's tangentiality argument: *Intervet*, 617 F.3d 1282. There, the patent covered representative strains of "PCV-2," a type of porcine circovirus. The original claim more broadly covered freestanding open reading frames ("ORFs") that could "encompass ORFs from any organism," even though they were meant to "be derived from porcine circovirus." *Id.* at 1291. The amended claim covered ORFs "of porcine circovirus type II." *Id.* The Court's holding could have been written for this case: the "rationale for the amendment was to narrow the claimed universe of [binders] down to [hardening binders], and bore only a tangential relation to the question of which [binders] are and are not properly characterized as [hardening binders]." *Id.* at 1292. The panel's contrary holding is in conflict.

Two more recent decisions are similar.[4] In *Eli Lilly*, the panel held that an equivalent was tangential where "the reason for the amendment was not to cede other, functionally identical, pemetrexed salts," such as the equivalent in question, but was to avoid a particular piece of prior art. 933 F.3d at 1331. In this case, Amgen cannot be viewed as having surrendered other functionally identical

[4] Amgen raised these cases in a Rule 28(j) letter, ECF No. 103, but the panel did not address either one.

hardening binders when the purpose of the Markush group was to clarify that hardening binders are claimed.

Finally, in *Ajinomoto*, the panel first identified "[t]he objectively evident rationale for the amendment," which "was to limit the set of proteins within the claim's scope so that it no longer included the prior-art E. coli YfiK protein and, more generally, no longer allowed as wide a range of amino acid alterations." 932 F.3d at 1355. The accused equivalent was tangential because "the reason for the narrowing amendment—limiting the amino-acid makeup of the proteins included in one of the alternatives covered by the claim—is unrelated to differences among the several DNA sequences that encode a given protein." *Id.* Likewise here, amending the claims to exclude non-hardening binders is unrelated to claiming other (equivalent) hardening binders. ECF No. 54, at 52.

B. The Panel Decision Risks Creating An Improper Categorical Rule.

The panel's flawed equivalents analysis also has the unsettling risk of creating a categorical rule that conflicts with *Festo VIII* and is particularly harsh when applied to formulation patents like Amgen's.

As explained above, the doctrine of equivalents is built on the understanding that "the nature of language makes it impossible to capture the essence of a thing in a patent application." *Festo VIII*, 535 U.S. at 731. That is why, even when a narrowing amendment is made for reasons of patentability, the Supreme Court

refused to hold that such an amendment operates as a "complete bar" to equivalents. *Id.* at 737. There is instead a "presumption that the patentee has surrendered all territory between the original claim limitation and the amended claim limitation," *Festo IX*, 344 F.3d at 1367, but that presumption "is not … just [a] complete bar by another name." *Festo VIII*, 535 U.S. at 741.

The panel's decision threatens to resurrect the test rejected in *Festo VIII* and risks turning the presumption back into a "complete bar by another name." Left unaddressed, any time an equivalent appears in a cited prior art reference—a regular occurrence for formulation patents and excipients—a narrowing amendment will be assumed to have been made to avoid that equivalent, and the "presumption" becomes a "complete bar." That is irreconcilable with *Festo VIII*.

Without an analysis of the "objectively evident rationale" for the amendment, the patentee is *ipso facto* denied any opportunity to overcome the presumption by, for example, demonstrating that the rationale for the narrowing amendment could not have been "to avoid" prior art that *included the claimed excipients*. Slip Op. 23 (recognizing Amgen's argument). Applying the *Festo VIII* inquiry would have required grappling with this issue. If left in place, the panel decision risks hamstringing the ability of patentees to rebut the presumption of complete surrender. *Festo VIII*, 535 U.S. at 740. The Court should grant rehearing to avoid such a result and the uncertainty and confusion that could follow.

CONCLUSION

For the foregoing reasons, Amgen respectfully asks the Court to grant panel rehearing or, alternatively, rehearing en banc.

Date: February 13, 2020

Respectfully submitted,

By: /s/ Bradford J. Badke

Bradford J. Badke
Sona De
SIDLEY AUSTIN LLP
787 Seventh Avenue
New York, NY 10019
(212) 839-5300

Ryan C. Morris
Joshua J. Fougere
Lauren Cranford Katzeff
SIDLEY AUSTIN LLP
1501 K Street, N.W.
Washington, DC 20005
Telephone: (202) 736-8000

Counsel for Plaintiff-Appellant Amgen Inc.

Wendy A. Whiteford
Lois M. Kwasigroch
Eric M. Agovino
AMGEN, INC.
One Amgen Center Drive
Thousand Oaks, CA 91320
Telephone: (805) 447-0464

John D. Murnane
Joshua I. Rothman
Alicia A. Russo
VENABLE | FITZPATRICK
Venable LLP, 1290 Avenue of the Americas
New York, NY 10104-3800
Telephone: (212) 218-2100

ADDENDUM

United States Court of Appeals for the Federal Circuit

AMGEN INC.,
Plaintiff-Appellant

v.

AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK LLC, PIRAMAL HEALTHCARE UK LIMITED,
Defendants-Appellees

ZYDUS PHARMACEUTICALS (USA) INC., CADILA HEALTHCARE LTD., DBA ZYDUS CADILA,
Defendants-Cross-Appellants

2018-2414, 2019-1086

Appeals from the United States District Court for the District of Delaware in Nos. 1:16-cv-00853-MSG, 1:16-cv-00925-MSG, 1:17-cv-00183-MSG, 1:17-cv-00713-MSG, Judge Mitchell S. Goldberg.

Decided: January 7, 2020

BRADFORD J. BADKE, Sidley Austin LLP, New York, NY, argued for plaintiff-appellant. Also represented by SONA DE; LAUREN CRANFORD KATZEFF, JOSHUA JOHN FOUGERE, RYAN C. MORRIS, Washington, DC; ERIC MICHAEL AGOVINO, LOIS KWASIGROCH, WENDY A.

WHITEFORD, Amgen Inc., Thousand Oaks, CA; ALICIA ALEXANDRA ROSE RUSSO, Fitzpatrick, Cella, Harper & Scinto, New York, NY; JOHN DENNIS MURNANE, JOSHUA ROTHMAN, Venable LLP, New York, NY.

JACOB M. HOLDREITH, Robins Kaplan LLP, Minneapolis, MN, argued for defendants-appellees Amneal Pharmaceuticals LLC, Amneal Pharmaceuticals of New York LLC. Also represented by BRENDA L. JOLY, KELSEY MCELVEEN; OREN D. LANGER, New York, NY.

AARON BARKOFF, McAndrews, Held & Malloy, Ltd., Chicago, IL, argued for defendant-appellee Piramal Healthcare UK Limited. Also represented by ALEJANDRO MENCHACA.

STEVEN ARTHUR MADDOX, Maddox Edwards, PLLC, Washington, DC, argued for defendants-cross-appellants. Also represented by JEREMY J. EDWARDS, MATTHEW C. RUEDY, KAVEH SABA; CHRISTOPHER CASIERI, McNeely Hare & War LLP, Princeton, NJ; WILLIAM HARE, RENITA SYBIL RATHINAM, Washington, DC.

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

LOURIE, *Circuit Judge*.

Amgen appeals from the district court's judgment that Amneal Pharmaceuticals LLC and Amneal Pharmaceuticals of New York LLC (collectively, "Amneal") does not infringe claims 1, 2–4, 6, 8–12, and 14–18 of U.S. Patent 9,375,405 ("the '405 patent"), Piramal Healthcare UK Ltd. ("Piramal") does not infringe claims 1–6 and 8–20. Zydus Pharmaceuticals (USA) Inc. and Cadila Healthcare Ltd. (collectively, "Zydus") cross-appeals from the court's judgment that they infringe claims 1–4, 6, 8–9, 15–17, and 19 of the '405 patent. *Amgen Inc. v. Amneal Pharm. LLC*, 328 F. Supp. 3d 373 (D. Del. 2018) ("*Decision*"). We conclude

that the district court construed the claims incorrectly and erred in its analysis of infringement by Amneal. However, the court properly applied prosecution history estoppel to Amgen's arguments regarding Piramal and otherwise did not err in its fact findings for Zydus. Thus, we vacate and remand the district court's judgment as to Amneal and affirm with respect to Piramal and Zydus.

BACKGROUND

Amgen holds approved New Drug Application No. 21688 for Sensipar®, a formulation of cinacalcet hydrochloride used to treat secondary hyperparathyroidism in adult patients with chronic kidney disease who are on dialysis and to treat hypercalcemia in patients with parathyroid cancer and primary and secondary hyperparathyroidism. Amneal, Piramal, and Zydus each filed an Abbreviated New Drug Application (ANDA) seeking to enter the market with a generic version of Sensipar®, and Amgen brought suit against each ANDA filer in the District of Delaware alleging that the proposed ANDA products would infringe the '405 patent.

The '405 patent is directed to a rapid dissolution formulation of cinacalcet. Amgen asserted different claims against each defendant, but the parties stipulated that the infringement findings for claim 1 would extend to the majority of the remaining claims.[1] Stipulation and Proposed Order Regarding Infringement, *Amgen Inc. v. Aurobindo*

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[1] Four claims asserted below are absent from the stipulation: claims 6, 8, 18 and 20. For claims outside of the stipulation, the court provided specific reasoning for its noninfringement or infringement conclusions. Because each party in this appeal argues only about claim 1 and in view of the stipulation, we treat claim 1 as dispositive for all claims at issue.

Pharma Ltd., No. 1:16-cv-00853-MSG (D. Del. Mar. 23, 2018); J.A. 2805–08. Claim 1 recites:

> A pharmaceutical composition comprising:
>
> (a) from about 10% to about 40% by weight of cinacalcet HCl in an amount of from about 20 mg to about 100 mg;
>
> (b) from about 45% to about 85% by weight of a diluent selected from the group consisting of microcrystalline cellulose, starch, dicalcium phosphate, lactose, sorbitol, mannitol, sucrose, methyl dextrins, and mixtures thereof,
>
> (c) from about 1% to about 5% by weight of at least one binder selected from the group consisting of povidone, hydroxypropyl methylcellulose, hydroxypropyl cellulose, sodium carboxymethylcellulose, and mixtures thereof; and
>
> (d) from about 1% to 10% by weight of at least one disintegrant selected from the group consisting of crospovid[o]ne, sodium starch glycolate, croscarmellose sodium, and mixtures thereof,
>
> wherein the percentage by weight is relative to the total weight of the composition, and wherein the composition is for the treatment of at least one of hyperparathyroidism, hyperphosphonia, hypercalcemia, and elevated calcium phosphorus product.

A. Prosecution History

The prosecution history is particularly relevant to the instant appeal. The '405 patent issued from U.S. Patent Application 12/942,646 ("the '646 application"). As originally filed, the '646 application contained only one claim,

which recited a "pharmaceutical composition comprising an effective dosage amount of a calcium receptor-active compound and at least one pharmaceutically acceptable excipient, wherein" the composition achieved a specific dissolution profile. J.A. 9171. Amgen filed a Preliminary Amendment, which cancelled claim 1 and added new claims 2–24. Newly filed claim 2, which ultimately issued as claim 1, recited a pharmaceutical composition comprising specific ranges, by weight, of cinacalcet and various excipients:

> A pharmaceutical composition comprising:
>
> > (a) from about 10% to about 40% by weight of cinacalcet HCl;
> >
> > (b) from about 45% to about 85% by weight of a diluent selected from the group consisting of microcrystalline cellulose, starch, dicalcium phosphate, lactose, sorbitol, mannitol, sucrose, methyl dextrins, and mixtures thereof,
> >
> > (c) from about 1% to about 5% by weight of at least one binder; and
> >
> > (d) *from about 1% to 10% by weight* of at least one disintegrant,
>
> wherein the percentage by weight is relative to the total weight of the composition.

J.A. 9382 (emphasis added).

The Examiner rejected the claims under 35 U.S.C. § 103 over U.S. Patent 6,211,244 ("Van Wagenen") "as evidenced by" U.S. Patent 6,656,492 ("Kajiyama") in view of U.S. Patent 6,316,460 ("Creekmore") and U.S. Patent App. 2005/0147670 ("Hsu"). J.A. 9417. According to the Examiner, Van Wagenen disclosed a calcimimetic "acting on a parathyroid cell calcium receptor" that "can be used to treat diseases such a primary hyperparathyroidism and

secondary hyperparathyroidism," J.A. 9417–18, and, while Van Wagenen failed to disclose the required amounts of various excipients, Creekmore and Hsu taught those limitations.

In response to this Office Action, Amgen filed an amendment narrowing the cinacalcet limitation to recite "from about 10% to 40% by weight of cinacalcet HCl in an amount of from about 20 mg to about 100 mg" ("Cinacalcet Amendment"). J.A. 9433. In support of this amendment, Amgen explained that the now narrower range of cinacalcet would not have been obvious in view of the teachings of Van Wagenen, which taught a broader range that "would translate to 0.62 mg to 3100 mg for an average human." J.A. 9438–40.

After the Cinacalcet Amendment, the Examiner conducted a telephone interview with Amgen's counsel, and Amgen accepted an amendment proposed by the examiner ("Examiner's Amendment"). J.A. 9464. The Examiner's Amendment revised the binder and disintegrant limitations into their current, Markush group format. The Examiner then allowed the claims, stating that the closest prior art did not disclose or render obvious the "combination of components . . . in the amounts . . . set forth in claim 2." J.A. 9462.

Following the Notice of Allowance, Amgen filed a number of Requests for Continued Examination providing various additional references and updating the U.S. Patent and Trademark Office on the revocation of a related patent after opposition proceedings in the European Patent Office, J.A. 9472–509, 9643–659. The Examiner issued a Notice of Allowance after each Request. While the second of the Requests was pending, Amgen submitted a "Preliminary Amendment." J.A. 10701. This amendment recited the claims exactly as they were allowed but underlined the language that had been proposed by the Examiner in the Examiner's Amendment. In accompanying documentation,

Amgen remarked that "[t]hese amendments have not been made in response to a prior art rejection but rather to place the claims in proper format and to better define the claimed subject matter, including equivalents." J.A. 10707.

B. District Court Proceedings

In the district court litigation, the construction of the binder and disintegrant Markush groups was a key issue. Oddly, neither party sought construction of the binder and disintegrant groups during claim construction. But the proper construction of the Markush groups was placed at issue in the context of pretrial preparations. In its proposed pretrial order, Amgen argued that the Markush groups should be open to unrecited elements, but the district court disagreed. Relying on *Multilayer Stretch Cling Film Holdings, Inc. v. Berry Plastics Corp.*, 831 F.3d 1350 (Fed. Cir. 2016), the court held that "Amgen ha[d] not overcome the very strong presumption that the Markush groups for the binder and disintegrant elements are closed to unrecited binders and disintegrants." *Amgen Inc. v. Aurobindo Pharma, Ltd.*, No. 16-cv-853, 2018 WL 1061369, at *3 (D. Del. Feb. 27, 2018) ("*Pretrial Order*"). Amgen sought reargument on this claim construction issue, but the court again rejected its positions. *Amgen Inc. v. Amneal Pharm. LLC*, No. 16-cv-853, 2018 WL 1885664, at *7–8 (D. Del. Apr. 19, 2018) ("*Reargument Order*").

The district court held a bench trial on the issue of infringement.[2] The court held that Amneal and Piramal do

[2] While Amneal, Piramal, and Zydus each asserted counterclaims that the '405 patent is invalid, the court bifurcated the infringement and invalidity issues, and trial on the infringement issue proceeded first. *Decision*, 328 F. Supp at 377; *Reargument Order*, 2018 WL 1885664, at *1 n.2.

not infringe any claim of the '405 patent but found that Zydus infringes claims 1–4, 6, 8–9, 15–17, and 19.

First, the district court found that Amneal does not infringe the asserted claims because its product does not meet the binder and disintegrant limitations. As a binder, Amneal uses Opadry Clear YS-1-7006, a product that contains hydroxypropyl methylcellulose ("HPMC"), polyethylene glycol 400, and polyethylene glycol 8000. *Decision*, 328 F. Supp. 3d at 383. Although HPMC is a listed binder, the court found that Opadry itself is not, so Amneal does not literally meet the binder limitation. *Id.* at 384.

As a disintegrant, Amneal's product uses crospovidone, which is listed in the disintegrant Markush group. *Id.* Relying on its claim construction, however, the court found that Amneal's product does not meet the disintegrant limitation. *Id.* at 385.

Next, the district court found that Piramal does not infringe because it does not meet the binder limitation. Piramal uses pregelatinized starch, *id.* at 392, and Amgen argued that the cold-water soluble fraction of the starch is equivalent to povidone, a listed binder. The court rejected this argument as barred by prosecution history estoppel. *Id.* In the court's view, Amgen had narrowed its claims by accepting the Examiner's Amendment to exclude binders different from those listed in the Markush group. The court found the Examiner's reliance on the "combination of components" in the notice of allowance underscored that the Markush groups were added for patentability. *Id.* at 393.

In contrast, the district court found that Zydus's ANDA product infringes the asserted claims. At issue for Zydus was the function of the pregelatinized starch in its formulation. Zydus's ANDA states that the formulation uses pregelatinized starch as a diluent, and starch is listed in the diluent Markush group of claim 1. Zydus relied on testimony from Dr. Davies, Amgen's expert, that the cold-water

soluble fraction of pregelatinized starch could function as an unlisted binder, but the court disagreed, rejecting Dr. Davies's fraction opinion as lacking credibility. The court ultimately found that Zydus's ANDA product literally infringes claim 1. *Id.* at 399.

DISCUSSION

Amgen appealed from the district court's judgment that Amneal and Piramal do not infringe the '405 patent. Zydus cross-appealed from the district court's judgment that it infringed. When Zydus filed its notice of appeal, however, its defense and counterclaim that the '405 patent is invalid had not been resolved. As a preliminary matter, we consider whether we have jurisdiction over Zydus's appeal.

"This court's jurisdiction is governed by the final judgment rule." *Robert Bosch, LLC v. Pylon Mfg. Corp.*, 719 F.3d 1305, 1308 (Fed. Cir. 2013) (en banc). The rule "as applied to patent disputes arising under 28 U.S.C. § 1338, is set forth at 28 U.S.C. § 1295." *Nystrom v. TREX Co.*, 339 F.3d 1347, 1350 (Fed. Cir. 2003). We review "final decisions" from district courts, which are decisions that end litigation on the merits and leave nothing for the court to do but execute the judgment. *Id.* (quoting *Catlin v. United States*, 324 U.S. 229, 233 (1945) and citing *Coopers & Lybrand v. Livesay*, 437 U.S. 463, 467 (1978)). The district court expressly conditioned its infringement judgment here on the claims being found "valid and enforceable." Trial Order, *Amgen Inc. v. Amneal Pharm. LLC.*, No. 1:16-cv-00853-MSG (July 27, 2018), ECF No. 376; J.A. 2. According to its own terms, the judgment did not resolve the parties' dispute and was thus not a "final decision." *See* Final Judgment, *Amgen Inc. v. Amneal Pharm. LLC.*, No. 1:16-cv-00853-MSG (Oct. 9, 2018), ECF No. 405; J.A. 5059–60.

However, when questioned at oral argument about the jurisdictional defect in Zydus's appeal, Zydus represented that it would "give up" its invalidity defense and claim even

if infringement was affirmed. Oral Arg. at 20:23–33, http://oralarguments.cafc.uscourts.gov/default.aspx?fl=2018-2414.MP3. Zydus's representation effectively cures the jurisdictional defect in its notice of appeal because the contingency identified by the district court—Zydus's potential invalidity defense and claim—is nullified. Thus, the court's judgment resolves all claims for all parties and is a final decision within our jurisdiction. Accordingly, we have jurisdiction over both the appeal and cross-appeal under 28 U.S.C. § 1295(a)(1).

We now turn to the merits. In its appeal, Amgen challenges the district court's construction of the binder and disintegrant Markush groups in claim 1 and alternatively argues that even under the district court's constructions, the court's findings for Amneal and Piramal were in error. For its part, Zydus agrees with the court's claim constructions but challenges the court's factfinding that Zydus's ANDA product infringes the '405 patent claims. We first address the overarching claim construction issue and reach the other issues in turn.

A. Legal Standard

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 when, despite some supporting evidence, we are left with a definite and firm conviction that the district court was in error." *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1186 (Fed. Cir. 2014) (citing *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006)). "The burden of overcoming the district court's factual findings is, as it should be, a heavy one." *Polaroid Corp. v. Eastman Kodak Co.*, 789 F.2d 1556, 1559 (Fed. Cir. 1986). "Where there are two permissible views of the evidence, the

factfinder's choice between them cannot be clearly erroneous." *Anderson v. City of Bessemer City,* 470 U.S. 564, 574 (1985) (citing *United States v. Yellow Cab Co.*, 338 U.S. 338, 342 (1949)).

An infringement analysis requires two steps. *Clare v. Chrysler Grp., LLC*, 819 F.3d 1323, 1326 (Fed. Cir. 2016). First, the court construes the asserted claims. Claim construction is a question of law that may involve underlying factual questions. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 332 (2015). Here, the court's constructions of Markush limitations are based solely on the intrinsic evidence, so we review them *de novo*. *HTC Corp. v. Cellular Commc'ns Equip., LLC*, 877 F.3d 1361, 1367 (Fed. Cir. 2017). Second, the court determines whether the accused product meets each limitation of the claim as construed, which is a question of fact that we review for clear error. *Wright Med. Tech., Inc. v. Osteonics Corp.*, 122 F.3d 1440, 1443 (Fed. Cir. 1997).

"Whether prosecution history estoppel applies to limit the doctrine of equivalents is a question of law which we review *de novo*." *Pharmacia & Upjohn Co. v. Mylan Pharm., Inc.*, 170 F.3d 1373, 1376 (Fed. Cir. 1999) (citing *Wang Labs., Inc. v. Mitsubishi Elecs. Am., Inc.*, 103 F.3d 1571, 1578 (Fed. Cir. 1997)).

B. Claim Construction

Amgen first challenges the district court's construction of the binder and disintegrant Markush groups in, respectively, elements (c) and (d). The district court held both of these Markush groups to be closed. *Pretrial Order*, 2018 WL 1061369, at *3. In reaching this result, the court first compared claim 1 to that at issue in *Multilayer*, which similarly recited "comprising," followed by "consisting of" terminology. The court explained that, as in *Multilayer*, there was a "very strong presumption" that the Markush groups were closed to unrecited constituents. *Id.* at *2. At this point in the litigation, Amgen pointed the court only to the

use of the word "comprising" in the preamble to support its position, and the court found this insufficient to overcome the presumption of closure.

Amgen later moved for reargument, contending that the district court misunderstood its claim construction position. *Reargument Order*, 2018 WL 1885664, at *3–4. In that motion, Amgen focused on the claim's recitation of "at least one" disintegrant and binder before the "consisting of" terms in each claim. Relying on this language, it argued that "[s]o long as the weight percentage is met by one of the listed binders or disintegrants, the presence of an additional excipient that functions as a binder or disintegrant does not take Defendants' products outside the literal scope of the claims." J.A. 2585.

The district court first rejected Amgen's arguments as untimely raised. *Reargument Order*, 2018 WL 1885664, at *4. The court still considered the merits, however, and found Amgen's construction to be inconsistent with the prosecution history. Particularly noteworthy was the fact that, before the claims even contained the Markush group limitations, Amgen claimed "from about 1% to about 5% by weight of at least one binder" and "from about 1% to about 10% by weight of at least one disintegrant." *Id.* at *5. Considering the prosecution history, it found that the percentage amounts of binder and disintegrant were "critical to the invention and, therefore, not subject to a construction that results in their vitiation." *Id.*

In this appeal, Amgen argues that the district court erred in construing the binder and disintegrant Markush groups because neither group forecloses the use of unlisted binders or disintegrants. Amgen Br. 29. As it did before the district court, Amgen again cites the "comprising" and "at least one" language in the claim to support its position. According to Amgen, the "comprising" term renders the claim open-ended, even when other language restricts the scope of particular claim elements, and the "consisting of"

term here only applies to the group from which "at least one" binder or disintegrant must be selected. *Id.* at 30.

Amgen also contrasts the binder and disintegrant limitations with the diluent limitation, which lacks the "at least one" language. Amgen maintains that the "at least one" language would be meaningless if the groups are closed to additional binders and disintegrants and meaningless in view of the claim's recitations of "mixtures thereof" within the Markush groups. *Id.* at 32 (citing *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 951 (Fed. Cir. 2006)).

For additional support, Amgen argues from the specification and trial testimony that the lists of excipients in the Markush groups are not exhaustive and that excipients can have different functions in different formulations. As for the district court's reliance on *Multilayer* and similar cases, Amgen argues that its claims here are distinguishable from the claims at issue in those cases because of the "at least one" limitation.

In response, Amneal, Piramal, and Zydus argue that the district court's construction was correct. Each of these parties argues that the district court properly applied *Multilayer* and that Amgen failed to overcome the strong presumption that a claim term set off with "consisting of" is closed to unrecited elements. Amneal & Piramal Br. 34 (quoting *Shire Dev., LLC v. Watson Pharm., Inc.*, 848 F.3d 981, 984 (Fed. Cir. 2017)); Zydus Br. 23–24. Each party also argues that Amgen's claim construction would require the court to ignore the criticality of the weight ranges for the binder and disintegrant elements as evidenced by the prosecution history. Amneal & Piramal Br. 29; Zydus Br. 29.

We conclude that Amneal, Piramal, and Zydus read more into *Multilayer* and *Shire* than is properly found there. *Multilayer* and *Shire* did not hold broadly that, whenever "consisting of" Markush group language is

present in a particular claim limitation, even when the limitation follows a general claim transition phrase of "comprising," all components of an accused product that perform the general function of the particular limitation must meet the requirements of that limitation, thus precluding components outside the Markush group. No such issue was presented in those cases. Rather, each decision held only that the terms of a particular claim limitation that used "consisting of" Markush group language were restricted to members of the Markush group. Those decisions do not apply in this case, where the question is whether the "binder" or "disintegrant" claim limitations are written to preclude other binders and disintegrants in the claimed composition. We conclude that they are not.

In *Multilayer*, we considered a claim to multilayer stretch films:

> 1. A multi-layer, thermoplastic stretch wrap film containing seven separately identifiable polymeric layers, comprising:
>
> > (a) two identifiable outer layers, at least one of which having a cling performance of at least 100 grams/inch, said outer layer being selected from the group consisting of linear low density polyethylene, very low density polyethylene, and ultra low density polyethylene resins, said resins being homopolymers, copolymers, or terpolymers, of ethylene and alpha-olefins; and
> >
> > (b) five identifiable inner layers, with each layer being selected from the group consisting of linear low density polyethylene, very low density polyethylene, ultra low density polyethylene, and metallocene-catalyzed linear low density polyethylene resins; said resins are homopolymers, copolymers, or

> terpolymers, of ethylene and C_3 to C_{20} alpha-olefins;
>
> wherein each of said two outer layers and each of said five inner layers have different compositional properties when compared to a neighboring layer.

831 F.3d at 1353 (quoting U.S. Patent 6,265,055 col. 1 l. 43–col. 2 l. 3).

In construing this claim, we held that a product, to come within element (b), with its Markush group listing particular resins, could not have other resins in the five identified inner layers of such a product. *Id.* at 1358–61. This construction was dictated by the transitional phrase "consisting of," which "creates a very strong presumption that that claim element is 'closed' and therefore 'exclude[s] any elements, steps, or ingredients not specified in the claim.'" *Id.* at 1358 (quoting *AFG Indus., Inc. v. Cardinal IG Co.*, 239 F.3d 1239, 1245 (Fed. Cir. 2001)). We further recognized that a patentee could act as its own lexicographer to give "consisting of" an alternative, less restrictive meaning, "[b]ut to overcome the exceptionally strong presumption that a claim term set off with 'consisting of' is closed to unrecited elements, the specification and prosecution history must unmistakably manifest an alternative meaning." *Id.* (citing *Conoco, Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1359 n.4 (Fed. Cir. 2006)). We concluded that the presumption was not overcome. *Id.* at 1359–61. As a result, we held that dependent claim 10, which added a requirement that "at least one said inner layer" of claim 1's element (b) contain a resin not listed in element (b), was invalid because it was inconsistent with the independent claim. *Id.* at 1361–62.

The issue was framed by Multilayer solely in terms of interpreting element (b), without any reliance on the "comprising" language of the general transition phrase of claim 1. This court thus had no occasion to, and did not, consider the effect of that transition phrase. Nor was there

a question presented or decided about whether element (b) applied to all layers in the claimed film, even all inner layers. The only issue was whether element (b) by itself declared that each layer among the five inner ones was restricted to the listed resins. The *Multilayer* claim limitation required, in terms, that "each layer" among the identified inner layers be "selected from" the Markush group. The only question was the meaning of the "consisting of" language applicable to "each layer."

Shire presented this court with a similar construction issue, but for a pharmaceutical claim:

> 1. Controlled-release oral pharmaceutical compositions containing as an active ingredient 5-aminosalicylic acid, comprising:
>
> > a) an inner lipophilic matrix consisting of substances selected from the group consisting of unsaturated and/or hydrogenated fatty acid, salts, esters or amides thereof, fatty acid mono-, di- or triglycerides, waxes, ceramides, and cholesterol derivatives with melting points below 90° C., and wherein the active ingredient is dispersed both in said [sic] the lipophilic matrix and in the hydrophilic matrix;
> >
> > b) an outer hydrophilic matrix wherein the lipophilic matrix is dispersed, and said outer hydrophilic matrix consists of compounds selected from the group consisting of polymers or copolymers of acrylic or methacrylic acid, alkylvinyl polymers, hydroxyalkyl celluloses, carboxyalkyl celluloses, polysaccharides, dextrins, pectins, starches and derivatives, alginic acid, and natural or synthetic gums;
> >
> > c) optionally other excipients . . .

848 F.3d at 983 (quoting U.S. Patent 6,773,720 col. 6 ll. 7–30). In construing the (a) and (b) Markush groups, we explained that the "consisting of" language defined the groups and created a "very strong presumption" that the Markush groups were closed to additional elements not specified in the claim. *Id.* at 984 (citing *Multilayer*, 831 F.3d at 1358). We then focused on element (b), determined that the presumption was not overcome, and found that the presence of magnesium stearate in the outer hydrophilic matrix, an excipient not recited in the (b) Markush group, rendered the appellee's product noninfringing. *Id.* at 985–86.

As in *Multilayer*, the issue presented to and decided by this court was framed solely in terms of interpreting element (b), without any reliance on the "comprising" language of the general transition phrase of claim 1. This court thus had no occasion to, and did not, consider the effect of that transition language. Nor was there a question presented or decided about whether element (b) applied to all matrices or outer matrices in the claimed composition. Element (b) states that an outer matrix of the claimed composition "consists of" the compounds in the Markush group. The court considered the component of the appellee's product that was alleged to meet that outer matrix limitation. That component, by the terms of element (b), had to "consist of" of those compounds to meet that limitation. The court's reiteration of the normal restrictive meaning of the "consist[ing] of" language settled the infringement issue: the product did not meet element (b) because the component alleged to meet that limitation contained compounds other than the listed ones.

The decisive issue in this case is critically different from any issue decided in *Multilayer* or *Shire*. The issue is whether all binders or disintegrants in the claimed formulation are subject to the specific binder or disintegrant limitations. The answer, we conclude, is no. There is no language in Amgen's claim indicating that every binder or

disintegrant in the claimed formulation must be within the Markush groups. Instead, the claim recites "at least one" binder or disintegrant "selected from the group consisting of" various excipients. And the limitations merely require that those particular binders or disintegrants meet the specified weight-percentage requirements, which is not inconsistent with the overall composition containing other binders or disintegrants. The plain language of this claim requires "at least one" of the Markush members and certainly does not indicate that the *only* binders and disintegrants in the claimed formulation are those listed in the groups. And we do not see a sufficient basis for a different conclusion in the specification or in the prosecution history we have recited.

Importantly, we also have the "comprising" language. The term "comprising" is the standard transition term used to make clear that the claim does not preclude the presence of components or steps that are in addition to, though not inconsistent with, those recited in the limitations that follow. *See Wis. Alumni Research Found. v. Apple Inc.*, 905 F.3d 1341, 1348 n.8 (Fed. Cir. 2018); *Multilayer*, 831 F.3d at 1358. Here, for the reasons just stated, the language of the binder and disintegrant limitations is not inconsistent with the presence of binders and disintegrants beyond those identified in those limitations. Amgen's use of the "comprising" transition phrase reinforces the conclusion that the language of those limitations is best construed not to foreclose such additional binders and disintegrants. Thus, optional additional binders and disintegrants not recited in the Markush group may be included in the claimed formulation.

In short, this case involves a claim that uses a "comprising" transition phrase and one of the following limitations requires a component that "consists of" items listed in a Markush group and that meets the limitation's requirements for the component. Without more, such language is satisfied when an accused product contains a component

that is from the Markush group and that meets the limitation's requirements for the component. It does not forbid infringement of the claim if an additional component is present functionally similar to the component identified in the Markush group limitation, unless there is a further basis in the claim language or other intrinsic evidence for precluding the presence of such additional components. There is no such basis here.

Because the district court's claim constructions in this case excluded formulations with additional unlisted ingredients—binders, disintegrants, or otherwise—those constructions are incorrect. The district court relied on its construction for the disintegrant Markush group to find that Amneal's product did not meet this limitation. The court held that the presence of an additional, unlisted disintegrant rendered Amneal's product non-infringing. Because we have reversed the claim construction, we vacate and remand this finding. On remand, the court should consider whether Amneal's product meets the disintegrant limitation applying the corrected construction.

The court's remaining findings regarding Amneal and the other defendants do not depend on its constructions of the Markush groups and are separately addressed below.

C. Amneal's Product

Amgen next challenges the district court's specific non-infringement finding for both Amneal and Piramal. We consider its arguments for each appellee in turn.

Amgen asks us to reverse the district court's fact findings that Amneal's ANDA product does not meet the binder limitation. The literal infringement question for the binder limitation is straightforward: does Amneal's formulation contain "from about 1% to about 5% by weight of at least one binder selected from the group consisting of povidone, hydroxypropyl methylcellulose ["HPMC"], hydroxypropyl

cellulose, sodium carboxymethylcellulose, and mixtures thereof"? '405 patent col. 13 ll. 26–30.

Amneal's ANDA states that its product uses "Opadry" as a binder. *Decision*, 328 F. Supp. 3d at 383. It was undisputed below that Opadry is a composite product comprised of HPMC, polyethylene glycol ("PEG") 400, and PEG 8000. J.A. 3770:14–22; 3977:5–3978:13. By containing Opadry, Amneal's formulation necessarily contains HPMC. HPMC is a binder listed in the binder Markush group of claim 1, so, provided that Amneal's formulation contains from about 1% to about 5% HPMC, irrespective of whether PEG is present, the formulation literally meets the binder limitation of claim 1.

The district court's analysis was more complex. The district court considered whether Opadry was "literally HPMC." *Decision*, 328 F. Supp. 3d. at 383. The court then identified differences between Opadry and HPMC, including that "HPMC is a single molecule, whereas Opadry is a molecular dispersion" of HPMC, PEG 400 and PEG 8000; that HPMC is a powder while the "three ingredients in Opadry make a 'slurry'"; and that Opadry is "manufactured by a single company, Colorcon, using a proprietary method, whereas HPMC is not." *Id.* at 383–84. The court also found that Opadry acts as a wet granulation binder by "spreading and surrounding the drug and excipient particles, forming a granule from the outside, in," but HPMC, also a wet granulation binder, acts "by sticking different types of particles together, forming a granule from the inside, out." *Id.*

These factual findings may be sound and perhaps accurately recite the differences between HPMC and HPMC in the presence of PEG. But they are not relevant to the question here—whether Amneal's formulation contains a listed binder. HPMC is a listed binder, and HPMC is present in Amneal's formulation. There will of course be differences between HPMC alone as compared to Opadry, which is HPMC combined with PEG. But those differences

cannot alter the conclusion that HPMC is present in Amneal's formulation, even if it was added as a component of another commercially available product. The claim requires only that HPMC be present, not that HPMC's physical characteristics or function be unaffected by additional ingredients.

Because the district court erred in its analysis of the binder in Amneal's formulation, we vacate its finding that Amneal does not infringe the asserted claims because of the identity of Opadry. On remand, the court should consider whether Amneal's formulation contains "from about 1% to about 5% by weight" of HPMC, irrespective of the HPMC's pairing with PEG.

D. Piramal's Product

Amgen challenges the district court's noninfringement finding for Piramal for a different reason: the court's application of prosecution history estoppel. Piramal's product uses pregelatinized starch as a binder, which is not listed in the binder Markush group of claim 1. Amgen therefore argues under the doctrine of equivalents that pregelatinized starch has a native starch fraction that functions as a diluent and a cold water soluble fraction that functions as a binder.

The doctrine of equivalents is well-established in our jurisprudence. *See Eli Lilly & Co. v. Hospira, Inc.*, 933 F.3d 1320, 1329 (Fed. Cir. 2019) (collecting cases). While "[t]he scope of a patent is not limited to its literal terms but instead embraces all equivalents to the claims described," *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 732 (2002), prosecution history estoppel acts as a "legal limitation" on the doctrine, *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 30 (1997). "Estoppel arises when an amendment is made to secure the patent and the amendment narrows the patent's scope." *Festo*, 535 U.S. at 736. The burden falls on the patentee to "demonstrate[] that an amendment required during

prosecution had a purpose unrelated to patentability." *Warner-Jenkinson*, 520 U.S. at 40–41. "Where the [patentee] is unable to establish such a purpose, a court should presume that the purpose behind the required amendment is such that prosecution history estoppel would apply." *Id.* at 41.

The district court rejected Amgen's doctrine of equivalents argument as barred by prosecution history estoppel. During prosecution, the examiner rejected Amgen's claims for obviousness, and, in response, Amgen narrowed the amount of cinacalcet in the claim in an attempt to overcome the rejection. In the court's view, Amgen tried but "failed" to overcome the obviousness rejection. *Decision*, 328 F. Supp. at 392. The court noted that the Examiner did not allow the claims following this amendment, but, instead, proposed the Examiner's Amendment adding Markush groups to the binder and disintegrant limitations. The court opined that "[t]here would have been no need for the Examiner to propose an amendment if Amgen's [Cinacalcet] Amendment was sufficient." *Id*. Moreover, the court noted that the Examiner stated that the claims were being allowed because the closest prior art failed to disclose or render obvious the "combination of components and in the amounts" in the claim. *Id.* at 392–93. The court understood these statements in the prosecution history to indicate that the Examiner's Amendment was entered for substantial reasons relating to patentability.

Amgen first argues that the presumption of estoppel does not apply here because it did not narrow the binder or disintegrant limitations for reasons of patentability. Instead, it submits that the Cinacalcet Amendment alone was necessary to rebut the prior art. Amgen Br. 47. Amgen points to the absence of any statements by the Examiner about the Markush groups in particular and Amgen's own later statement in the second Request for Continued Examination that the language added by the Examiner was not added in "response to a prior art

rejection but rather to place the claims in proper format and to better define the claimed subject matter, including equivalents." Amgen Br. 49 (quoting J.A. 10707).

Even if the presumption of estoppel applies, however, Amgen argues that it is overcome because the Markush limitations were added for reasons other than patentability. Amgen argues that the Examiner's Amendment simply explained in more explicit terms and clarified the composition that the claims already covered. Because the Markush groups and treatment limitations were already present in previously rejected dependent claims, Amgen argues that a person of skill would have understood from the intrinsic record that the Examiner's Amendment was not related to patentability. According to Amgen, the amendment could not have distinguished Creekmore or Hsu because those references already disclosed the excipients in the Markush groups.

Piramal responds that Amgen's acceptance of the Examiner's Amendment led directly to the allowance of the claims. Amneal & Piramal Br. 49. According to Piramal, Amgen's statement during prosecution that its amendment was not in response to a prior art rejection was self-serving and is irrelevant to whether a claim amendment was made for reasons of patentability. *Id.* at 50. In Piramal's view, the Examiner's Amendment was substantial and narrowed the claims, so it could not be considered a clarifying amendment. Piramal also argues that the addition of the Markush groups overcame the obviousness rejection. Piramal reads Creekmore to disclose 152 binder-disintegrant combinations and Hsu discloses 120 combinations. Thus, Piramal submits that the narrowed range of excipient combinations in the Examiner's Amendment—which would include only 12 disintegrant-binder combinations—overcame Creekmore and Hsu because the amended claim recited a smaller set of members within the group. *Id.* at 54.

We agree with Piramal that Amgen's doctrine of equivalents argument is barred by prosecution history estoppel. Amgen amended its claims in two ways during prosecution—first narrowing the amount of cinacalcet to a range of 20 mg to 100 mg and second, accepting an Examiner's Amendment that revised the claim's disintegrant and binder limitations to be in Markush group format. Amgen urges that only the first of these amendments, the Cinacalcet Amendment, was adopted for a substantial reason relating to patentability. But if Amgen is correct that its narrowing of the cinacalcet limitation was sufficient to secure allowance, the Examiner proposed the Examiner's Amendment for no purpose at all. Such a reading of the prosecution history is at best unpersuasive.

Amgen also points to its statement in its second Request for Continued Examination that the Examiner's Amendment was added "to place the claims in proper format and to better define the claimed subject matter." Amgen Br. 49 (citing J.A. 10707). But this statement was made over eight months after the Examiner's Amendment was accepted and the claims were allowed. It is unclear what, if any, insight this conventional boilerplate statement provides into the reasons for the Examiner's Amendment.

We therefore conclude that Amgen failed to carry its burden to demonstrate that the Examiner's Amendment was made for a reason unrelated to patentability. We thus agree that Amgen surrendered equivalent but unclaimed binders and disintegrants. *Warner-Jenkinson*, 520 U.S. at 41. It is estopped to claim equivalence to remedy a failure of the accused product to meet the Markush limitations.

As a final argument, Amgen suggests that the tangential exception to prosecution history estoppel applies. However, Piramal uses pregelatinized starch as a binder, a use taught by Creekmore and Hsu. "[A]n amendment made to avoid prior art that contains the equivalent in question is

not tangential." *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1291 (Fed. Cir. 2010).

E. Zydus's Product

In its cross-appeal, Zydus asks us to reverse the district court's finding that Zydus's product infringes the '405 patent. At issue here is the starch in Zydus's formulation. As the district court noted, Zydus's ANDA states that the pregelatinized starch in Zydus's formulation functions as a diluent. But starch is listed in the diluent Markush group of claim 1, so, if the starch in Zydus's formulation truly functions as a diluent, Zydus infringes claim 1.

Before the district court, Amgen argued that pregelatinized starch in Zydus's formulation functions as a diluent, but Zydus argued that the starch functions as a binder. To support its position, Zydus adopted the testimony of Dr. Davies, Amgen's expert, that Amgen had proffered for its argument about Piramal's formulation. Dr. Davies opined that pregelatinized starch's native starch fraction functions as a diluent but that its cold water soluble fraction functions as a binder.

The district court did not find Dr. Davies's testimony credible for several reasons. For example, the court first found that Dr. Davies's opinion was inconsistent between defendants. For Aurobindo[3] and Piramal, Dr. Davies provided his fractions opinion regarding the function of pregelatinized starch, but for Zydus, Dr. Davies simply accepted Zydus's identification in its ANDA that pregelatinized starch functions as a diluent. At trial, Dr. Davies modified his opinion and testified that he was also applying his

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[3] Amgen also accused Aurobindo Pharma Ltd. and Aurobindo Pharma USA, Inc. (collectively, "Aurobindo") of infringing the '405 patent, and Amgen's claims against Aurobindo were tried alongside its claims against Amneal, Piramal, and Zydus but are not at issue in this appeal.

fractions opinion to Zydus. As a result, Dr. Davies testified that Zydus's product, which already uses 4.98% of hydroxypropyl cellulose as a binder, also includes 3.97% of pregelatinized starch as a binder. Dr. Davies thus opined that Zydus's formulation contains 8.95% by weight of binder, which exceeds the "about 5%" binder limitation in claim 1. When this opinion was challenged, Dr. Davies provided a third opinion that was inconsistent with the court's claim construction.

The district court also discounted Dr. Davies's testimony because, while he consistently asserted that the function of pregelatinized starch was context-specific and could vary based on the amount of pregelatinized starch, other excipients present, and the manufacturing process, he did not provide testimony applying those contextual factors to each ANDA product. The court contrasted Dr. Davies's testimony with that of Aurobindo's expert, Dr. Fassihi, and Amneal's expert, Dr. McConville, who did provide such analysis.

Because the district court ultimately did not credit Dr. Davies's fraction opinion concerning pregelatinized starch, it rejected Zydus's noninfringement argument. The court thus found that Zydus's ANDA product infringed claim 1.

Zydus now argues on appeal that Amgen failed to prove that pregelatinized starch is a listed binder in Zydus's product. Zydus again cites Dr. Davies's fraction opinion and testimony that pregelatinized starch functions as a second binder in Zydus's product. According to Zydus, the district court required Zydus to disprove infringement, contrary to this court's precedent. Zydus further contends that the court's consideration of testimony from other defendants' experts in evaluating Zydus's products was improper because it amounts to comparing the accused products to one another. Zydus Br. 42.

Amgen responds that it met its burden to show infringement. According to Amgen, it presented the district

court with Zydus's ANDA, which explicitly discloses that Zydus's product uses pregelatinized starch as a diluent. Amgen points further to Dr. Davies's testimony that the starch in Zydus's product functions as a diluent. Amgen suggests that the court was free to credit some aspects of Dr. Davies's testimony and reject others, which it chose to do here.

We agree with Amgen that the district court did not clearly err in finding that the pregelatinized starch in Zydus's product functions as a diluent. Zydus thus is an infringer. Dr. Davies undoubtedly provided a wide range of opinions regarding the starch in Zydus's product. But the district court repeatedly identified problems in Dr. Davies's "fractions opinion," but not in his opinion that the pregelatinized starch in Zydus's product functions only as a diluent. And the court was not required to reject all of Dr. Davies's testimony once finding any individual part of it incorrect. *See Bluebonnet Sav. Bank, F.S.B. v. United States*, 466 F.3d 1349, 1359 (Fed. Cir. 2006) (quoting *White Mountain Apache Tribe of Arizona v. United States*, 11 Cl. Ct. 614, 663 (1987)). Thus, the court was permitted to rely on Dr. Davies's initial opinion that the pregelatinized starch in Zydus's product functions as a diluent. *See* J.A. 3433:23–3434:5. And, expert testimony aside, the court was certainly permitted to credit the statements in Zydus's own ANDA that the starch in its product functions as a diluent.

Zydus's argument that the district court incorrectly compared the accused products is unfounded. In evaluating whether Dr. Davies's testimony was credible, the court was entitled to consider the record, including testimony from other experts regarding the multifunctional nature of excipients, before reaching its conclusion. At no point, however, did the court compare Aurobindo's or Piramal's products to Zydus's in its analysis.

CONCLUSION

We have considered the parties' remaining arguments but find them unpersuasive. Accordingly, the district court's judgment that Amneal does not infringe claims 1, 2–4, 6, 8–12, and 14–18 of the '405 patent is vacated and remanded for further proceedings consistent with this opinion. The district court's judgment that Piramal does not infringe claims 1–6 and 8–20 of the '405 patent and that Zydus infringes claims 1–4, 6, 8–9, 15–17, and 19 of the '405 patent is affirmed.

AFFIRMED-IN-PART, REVERSED-IN-PART, VACATED-IN-PART, AND REMANDED

COSTS

No costs.

CERTIFICATE OF SERVICE

I hereby certify that on February 13, 2020, a true and correct copy of the foregoing was timely filed with the Clerk of the Court using the appellate CM/ECF system, which will send notifications to all counsel registered to receive electronic notices.

/s/ Bradford J. Badke
Bradford J. Badke

CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitations of Federal Rules of Appellate Procedure 40(b) and 35(b)-(c) and the Rules of this Court, because it contains 3,433 words (as determined by the Microsoft Word word-processing system used to prepare the brief).

This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(c)(2) and the type-style requirements of Federal Rule of Appellate Procedure 32(c)(2) because it has been prepared in a proportionally spaced typeface using the Microsoft Word word-processing system in 14-point Times New Roman font.

/s/ Bradford J. Badke

Bradford J. Badke
SIDLEY AUSTIN LLP
787 Seventh Avenue
New York, NY 10019
(212) 839-5300

Counsel for Plaintiff-Appellant Amgen Inc.