IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF PENNSYLVANIA

AMGEN INC. and AMGEN MANUFACTURING LIMITED,	)	Civil Action
	)	
	)	No. 17-cv-01235-MRH
Plaintiffs,	)	
	)	
v.	)	**REDACTED VERSION**
	)	
MYLAN INC., MYLAN PHARMACEUTICALS INC., MYLAN GMBH and MYLAN N.V.,	)	***Electronically Filed***
	)	
	)	
Defendants.	)	

AMGEN'S RESPONSE IN OPPOSITION TO MYLAN'S MOTION FOR JUDGMENT ON THE PLEADINGS PURSUANT TO RULE 12(c) REGARDING U.S. PATENT NO. 8,273,707

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I. INTRODUCTION

The parties agree that in evaluating Mylan's Motion for Judgment on the Pleadings ("Motion"), the court must "accept all of the complaint's well-pleaded facts as true," and that the motion is denied if "the facts alleged in the complaint are sufficient to show that the plaintiff has a 'plausible claim for relief.'" D.I. 81 ("Mylan Br.") at 14-15. The parties also agree that the court may consider "not only the pleadings" but also U.S. Patent No. 8,273,707 ("the '707 Patent"), Mylan's abbreviated Biologics License Application ("aBLA") describing the accused manufacturing process, and the '707 Patent prosecution history. Mylan Br. at 3, 15-16. Mylan also appears to agree that Amgen's detailed statement regarding infringement—provided to Mylan during the pre-Complaint information exchanges under 42 U.S.C. § 262(*l*)(3)(C) of the Biologics Price Competition and Innovation Act ("BPCIA) ("Amgen's 3(C) Statement")—must be considered because Mylan discusses and attaches an excerpt of those "contentions" as Exhibit 9 to its brief (D.I. 81-9). Mylan Br. at 3, 14, 16, 23.

Thus, the dispositive question here is whether Amgen has alleged facts in its Complaint and 3(C) Statement that are sufficient to show a plausible claim for relief for infringement of the '707 Patent. The answer is "yes." The sole claim limitations that Mylan's Motion asserts are not met in Mylan's process are the requirements that (1) the protein be mixed with "a combination of a first salt and a second salt" "wherein the first and second salts are selected from the group consisting of citrate and sulfate, citrate and acetate, and sulfate and acetate"; and (2) "the concentration of each of the first salt and the second salt in the mixture is between about 0.1 M and about 1.0 [M]." Mylan Br. at 16. Amgen's Complaint and 3(C) Statement each allege that these limitations are met and Amgen's 3(C) Statement sets forth facts that support these allegations. This ends the inquiry; Mylan's Motion should be denied.

First, Amgen alleges that Mylan's manufacturing process uses a [redacted]. Ex. 1 (Amgen's (3)(C) Statement) at 35. Mylan admits, as it must, that its [redacted]. Mylan Br. at 21. Mylan asserts [redacted] *id.*, but the first question is simply whether one of the salt pair combinations recited in the claims of the '707 Patent is literally present. [redacted] the answer is plainly "yes." [redacted] Ex. 1 (Amgen's (3)(C) Statement) at 34-35 (emphases added). [redacted]

Nevertheless, Mylan asks this Court to disregard Amgen's allegations arguing that the claim must be construed so that the mixing ends "prior to loading." Mylan Br. at 16, 20-21. Amgen disputes that the claim is so limited; nothing in the claim language itself requires that the mixing be completed before loading. Rather, as Amgen has alleged, [redacted] Ex. 1

(Amgen's (3)(C) Statement) at 34-35. [redacted] *Id.* In any event, the Court need not (and should not) resolve this claim construction dispute in deciding Mylan's motion. As the Federal Circuit recently held in *Nalco Co. v. Chem-Mod., LLC*, resolution on the pleadings is not appropriate when the "proper scope" of an asserted claim is disputed; it is also not appropriate when factual findings are required. 883 F.3d 1337, 1348-49 (Fed. Cir. 2018). The same result is appropriate here.

Second, Amgen alleges that [redacted] Specifically, the concentrations of each of the salts, in combination with another salt, "will be shown to increase the dynamic capacity of [Mylan's column] for [the protein]." Ex. 1 (Amgen's (3)(C) Statement) at 37-38. As an initial matter, there is a claim construction issue as to what "about 0.1 M" means which requires evidence as to how one of ordinary skill in the art would understand that term. It cannot be resolved now, on a motion for judgment on the pleadings. Further, Mylan's argument that Amgen surrendered claims to processes using salt concentrations lower than 0.1 M fails. The sole basis for Mylan's argument is statements that Amgen made to the Patent Office about ***different claims involving a different salt pair*** than the claims-at-issue here. *See* Mylan Br. at 23-24. Because these statements are directed to "citrate and phosphate" subject matter that differs from the claims at issue here, they cannot (and do not) bar Amgen from asserting infringement under the doctrine of equivalents here. *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052, 1078 (Fed. Cir. 2005) (parent application does not limit different claim language in a continuation application); *Biogen, Inc. v. Berlex Labs, Inc.*, 318 F.3d 1132, 1141 (Fed. Cir. 2002) (estoppel does not arise from prosecution of different claims in divisional application).

Finally, the Delaware district court decision finding non-infringement of the '707 Patent does not control the outcome here. Mylan Br. at 10-12 (citing *Amgen Inc. v. Coherus Biosciences, Inc.*, No. 17-546-LPS-CJB, 2018 WL 1517689 (D. Del. March 26, 2018). That case addressed Amgen's infringement allegations with respect to a ***different*** manufacturing process by a ***different*** biosimilar company (Coherus). While the details of the accused Coherus process are confidential (including the particular salt pairs used in the process), there is no dispute that Amgen's allegations in that case are ***different*** than the ones pled here. Unlike in *Coherus*, Amgen alleges here that the salt pair limitation is literally met here because [redacted] That was not the case in *Coherus*. *See Coherus Biosciences Inc.*, 2018 WL 1517689, at *4. The Delaware court was not asked to decide (and did not decide) whether the Mylan manufacturing process using [redacted] literally satisfies the '707 Patent claims. Further, this Court cannot resolve the parties' disputes here based on the *Coherus* court's dismissal of Amgen's allegations that a presumably different salt pair used by Coherus is equivalent to the claimed salt pairs. In addition, the Delaware court did not address whether the particular salt pairs used by *Coherus* meet the concentration limitation. *Id.* at *3 n.4.

Accordingly, Amgen respectfully requests that Mylan's Motion be denied.

II. ARGUMENT

A. Amgen's Allegations in Its Complaint and 3(C) Statement, Which Must Be Accepted as True, State More Than a "Plausible Claim for Relief"

The parties agree that Mylan's Motion fails if Amgen has pled a facially plausible claim, *i.e.*, pled "factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009); *see Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555-56 (2007). Indeed, judgment on the pleadings is ***not*** appropriate even if "it strikes a savvy judge that actual proof of those facts is improbable."

Twombly, 550 U.S. at 556. The parties also agree that Amgen's allegations must be taken as true, and that documents "integral to or explicitly relied upon in the Complaint" may be considered in resolving Mylan's Motion. Mylan Br. at 15. Specifically, the parties agree that the '707 Patent, the aBLA, and the '707 Patent prosecution history are part of the record here. *Id.* at 15-16. And so is Amgen's 3(C) Statement, which Mylan discusses in its Brief and attached as an excerpt, Mylan's Exhibit 9 (D.I. 81-9).[1] *Id.* at 14, 16, 23. Amgen's Complaint explicitly relies on the 3(C) Statement, which Amgen provided to Mylan during the BPCIA information exchanges before filing the Complaint. The only reason that Amgen did not recite the allegations of its (3)(C) Statement is because Amgen is not permitted to include confidential information provided by Mylan GmbH "in any publicly-available complaint or other pleading" under the BPCIA. D.I. 1 ¶ 89; *see* 42 U.S.C. § 262(*l*)(1)(F).

Amgen's Complaint and its 3(C) Statement allege facts of infringement, which must be credited as true. D.I. 1 ¶ 90; Ex. 1 (Amgen's (3)(C) Statement) at 33-38. Mylan now asserts that two limitations in the '707 Patent claims are not met: (1) mixing a preparation containing the protein with a combination of a first salt and a second salt selected from the group consisting of "citrate and sulfate, citrate and acetate, and sulfate and acetate" (highlighted in yellow); and (2) the concentration of each of the first salt and the second salt in the mixture is between about 0.1 M and about 1.0 M (highlighted in green).

> A process for purifying a protein on a hydrophobic interaction chromatography column such that the dynamic capacity of the column is increased for the protein comprising mixing a preparation containing the protein with a combination of a

[1] Mylan cites to an excerpt from Amgen's Contentions and attaches it as Exhibit 8. *See* Mylan Br. at 12, 14, 16. Amgen's Contentions are not part of the Complaint. *See* Ex. 2 (Amgen's Contentions) at 4. To the extent the Court considers those materials and treats Mylan's Motion as a motion for summary judgment, the Motion fails because Amgen's factual allegations must be credited as true. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1304 (Fed. Cir. 1999); *see also Big Apple BMW, Inc. v. BMW of N. Am., Inc.*, 974 F.2d 1358, 1363 (3d Cir. 1992).

> first salt and a second salt, loading the mixture onto a hydrophobic interaction chromatography column, and eluting the protein, wherein the first and second salts are selected from the group consisting of citrate and sulfate, citrate and acetate, and sulfate and acetate, respectively, and wherein the concentration of each of the first salt and the second salt in the mixture is between about 0.1 M and about 1.0 [M].

D.I. 81-2 ('707 Patent) claim 1. Each of Mylan's arguments fails.

1. The '707 Patent

The '707 Patent is directed to a process for protein purification using hydrophobic interaction chromatography, or "HIC." D.I. 81-2 ('707 Patent) at col. 1, lines 13-15. Chromatography is a method of purifying a protein wherein the protein is separated from impurities based on the protein's chemical and/or physical properties. *See id.* at col. 1, lines 29-35. HIC separates a protein from impurities based on a property known as hydrophobicity. *Id.* at col. 1, lines 36-49. In HIC, a liquid mixture containing the protein, known as the "solution phase" or "mobile phase," is passed through a column containing a solid matrix, known as the "solid phase" or "resin," which is covered with immobilized hydrophobic groups. *See id.* at col. 3, lines 7-12, 53-64. Hydrophobic regions on the surface of the protein interact with the hydrophobic groups on the matrix in the column, and this interaction causes the protein to bind to the matrix while impurities flow past and out of the column. *See id.* Salt(s) in the mobile phase facilitate hydrophobic interactions between the protein and the matrix and thereby facilitate protein binding to the HIC matrix. *Id.* at col. 1, lines 40-49. Elution (*i.e.*, release) of the protein from the column is typically achieved by reducing the salt concentration in the mobile phase to reverse the binding of the protein from the matrix. *See id.* at col. 3, 13-16.

The '707 Patent addresses an issue known as "'breakthrough' or loss of protein to the solution phase before elution." *See id.* at col. 2, lines 9-20. The invention improves processes known at the time by increasing a HIC column's "dynamic capacity," which is the maximum amount of protein in solution which can be loaded onto a column without significant

breakthrough or leakage of the protein into the solution phase of the column before elution. *Id.* at col. 3, lines 6–col. 4, line 3. Before the '707 Patent, HIC purification relied on high salt concentrations to increase dynamic capacity. *See id.* at col. 3, lines 37-41. But high concentrations of salt can be detrimental. *Id.* at col. 3, lines 41-45. A key inventive aspect of the '707 Patent is the use of a combination of a first salt and a second salt, each at a relatively low concentration, that together "increase the dynamic capacity of the HIC column for a particular protein" more than using a single salt alone at the high concentrations reported in the prior art. *See id.* at col. 4, lines 46-51, col. 5, lines 26-28; *see also id.* at col. 2, lines 9-15; col. 4, lines 33-42, 56-60; col. 5, lines 25-26; col. 15, line 8–col. 16, line 26. By increasing the dynamic capacity of a HIC column and using a lower salt concentration, the invention improves the efficiency of the HIC purification process. *See id.* at col. 1, lines 54-62. This then decreases the cost and time required to purify a batch of protein, which is particularly useful in commercial production and purification of proteins, especially therapeutic proteins, such as G-CSF. *See id.* at col. 10, line 4-24; col. 11, lines 36-46.

2. In Mylan's Process, a Preparation Containing Protein Is Mixed With a Claimed Combination of a First Salt and a Second Salt

a. Mylan's Process Uses a Mixture of [redacted] Which Literally Meets the Claim Limitation

Amgen alleges that when Mylan [redacted] Ex. 1 (Amgen's (3)(C) Statement) at 34-35; Ex. 2 (Amgen's Contentions) at Appx. A 1-2, 5-8. [redacted]

[redacted]. Ex. 1 (Amgen's (3)(C) Statement) at 34-35; Ex. 2 (Amgen's Contentions) at Appx. A 1-2, 5-8. [redacted] *See In re Omeprazole Patent Litigation*, 536 F.3d 1361, 1376 (Fed. Cir. 2008) (a subcoating that forms in situ can be "disposed on said core region").

Mylan's Brief acknowledges that Amgen's infringement allegations must be taken as true, but then asks this Court to ignore the facts alleged in Amgen's 3(C) Statement. Mylan Br. at 14. With respect to the salt pair limitation, Amgen's 3(C) Statement asserts:

> Claim 1 is directed to the use of a combination of salts, including citrate and acetate, sulfate and acetate, and citrate and sulfate. '707 Patent at col. 15:15-16. [redacted]

[redacted]

Ex. 1 (Amgen's (3)(C) Statement) at 34-35 (emphasis added). These factual allegations must be credited as true and all reasonable inferences made in Amgen's favor in resolving this Motion.

Mylan asserts that Amgen's allegations should be dismissed because the '707 Patent requires that the claimed mixing be completed "prior to loading." Mylan Br. at 4-5, 16, 20-21. According to Mylan, the claimed salt pair combination must be found in the [redacted] *Id.* at 12-13. This is a claim construction argument which improperly interprets the claims to require that the mixing be completed at a particular time ("prior to loading") with these particular components. Nothing in the claims so requires, and Mylan cannot import limitations into the claims. *See Interactive Gift Express, Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1342-43 (steps in a method claim "are not ordinarily construed to require" an order).

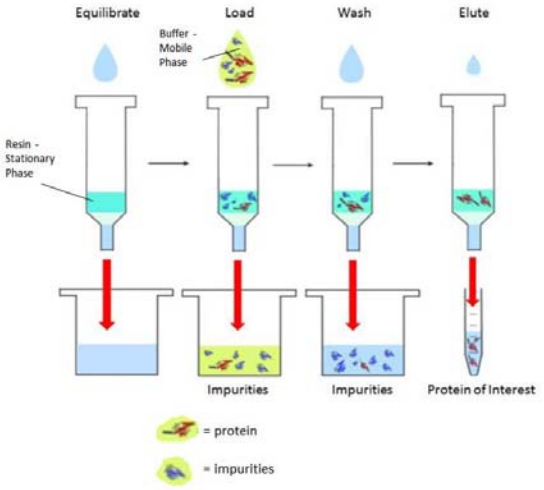
Mylan relies on a claim construction decision—*Mformation Technologies, Inc. v. Research in Motion,* 764 F.3d 1392, 1398-99 (Fed. Cir. 2014)—to assert otherwise. Mylan Br. at 20. In that case, the Federal Circuit affirmed a construction that a connection be established between the wireless device and the server before information is transmitted from the wireless

device to the server. *Mformation Techs., Inc.*, 764 F.3d at 1399. The Federal Circuit reasoned that "establishing a connection is necessarily encompassed in transmitting a command," and "[a]s a matter of logic, a mailbox must be established before the contents of said mailbox can be transmitted." *Id.* at 1399-1400. That is not the case here where the patent claims and specification do not dictate when mixing occurs; all that is required is that mixing happen. *See* '707 Patent, claim 1. It follows that mixing [redacted] More fundamentally, it is inappropriate for this Court to resolve claim construction disputes in deciding Mylan's Motion. *See Nalco Co.*, 883 F.3d at 1349-50. At the very least, the Court should have the benefit of the procedure and the party's briefing as scheduled for claim construction in this case.

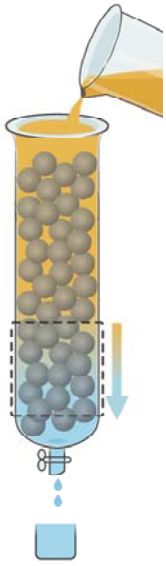
Nor would it be appropriate for the Court to resolve disputed material facts in Mylan's favor at the pleading stage. *Id.* Amgen has alleged that [redacted]. It would be reasonable to infer from the allegations appropriately considered here, that as [redacted] Mylan apparently disputes these facts. For example, [redacted]

[redacted]

Figure 1 of Mylan's Motion



Amgen's Illustration [redacted]



In Amgen's illustration, the blue at the bottom of the column represents the solution in the column when another solution, the yellow solution, is added. For example, [redacted] Even in the Delaware decision that Mylan quotes, it is the interaction between the load solution and the column matrix that is considered loading: "The interaction between the matrix material and loading solution causes the proteins to adhere to the matrix as the solution flows through the matrix. This step in the HIC process is known as 'loading' the mixture onto the column." *See* Mylan Br. at 4-5 (quoting D.I. 81-1 at 2). Loading is not the mere act of pouring a solution into the column. The conditions in the column change over time as the load solution and other solutions are added; the protein interacts with and binds the matrix while other materials are carried away (eluted) as a result of these changing conditions. Amgen expects that evidence as to this factual dispute will be the subject of discovery in this case, and it is not appropriate for the Court to resolve this factual dispute regarding Mylan's process here.

Mylan asserts prosecution history estoppel bars "Amgen from asserting [literal] infringement." *Id.* at 21. According to Mylan, [redacted]. *Id.* Mylan then argues that Amgen is estopped from asserting infringement against a process that uses "more salts than the two-salt system." *Id.* Mylan misunderstands the law of prosecution history estoppel, which applies to bar the application of the doctrine of equivalents. Prosecution history estoppel does not apply to bar literal infringement and does not prevent Amgen from arguing that Mylan's [redacted]

[redacted] that infringe the asserted claims. *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 870 (Fed. Cir. 1985) ("Prosecution history estoppel applies as a limitation to the doctrine of equivalents *after* the claims have been properly interpreted and no literal infringement is found." (emphasis in original)), *overruled on unrelated grounds by Nobelpharma AB v. Implant Innovations, Inc.*, 141 F.3d 1059, 1067-68 (Fed. Cir. 1998).

Further, Mylan cites *Ormco Corp. v. Align Tech., Inc.*, 498 F.3d 1307, 1314 (Fed. Cir. 2007) and *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1333 (Fed. Cir. 2003) for the proposition that "prosecution disclaimer may arise from disavowals made during the prosecution of ancestor patent applications." Mylan Br. at 22. Mylan misapprehends prosecution disclaimer which is a separate and distinct doctrine from prosecution history estoppel. Unlike prosecution history estoppel which applies to bar doctrine of equivalents claims, prosecution disclaimer guides claim interpretation. *Trading Techs. Int'l, Inc. v. Open E Cry, LLC*, 728 F.3d 1309, 1322-23 (Fed. Cir. 2013). Prosecution disclaimer does not apply here because claim construction issues are not resolved at the pleading stage; interpreting those statements are the types of "classic *Markman* arguments" that address the scope of the claims and that require a fully developed record to resolve. *See Nalco Co.*, 883 F.3d at 1349.

In any event, Mylan's argument that the claims exclude [redacted] fails. According to Mylan, Amgen "explicitly disclaimed solutions that contain more salts than the two-salt system." Mylan Br. at 21. This is incorrect. During the '707 Patent prosecution, Amgen distinguished a prior art reference, U.S. Patent No. 5,231,178 ("Holtz") as not disclosing a combination of the particular claimed salts, and also not disclosing, suggesting, or contemplating any steps "involving a combination of two salts for any purpose whatsoever." Ex. 5 at 54 ('707 Patent FH, 8/22/2011 Reply to OA of 4/7/2011 at 5). Amgen also stated that

Holtz "merely teaches a standard salt in HIC chromatography—adding a high concentration of ammonium sulfate to a low concentration of a buffer solution to prepare a protein for a HIC column" and that Holtz "does not even make reference [to] a 'single salt system.'" *Id.* Amgen said however that "to the extent Holtz et al applied a salt in a HIC operation, it was a single salt and it was used in at traditional and well-established capacity, namely to alter the hydrophobic interactions in a buffered salt-containing solution so as to induce the target protein to associate with the HIC column matrix." *Id.* at 55 ('707 Patent FH, 8/22/2011 Reply to OA at 6).

In the parent application prosecution, Amgen referred to Holtz as "a protein solution containing lower concentrations of sodium acetate and sodium phosphate, together with NaCl and a high concentration of ammonium sulfate (four salts, not a combination of two salts)." Amgen then distinguished Holtz as not teaching combining the protein with a "*particular combination of two salts, citrate and phosphate salts*, at concentrations of between about *0.1M* and *1.0M* before loading the protein on the HIC column." Ex. 9 at 7-8 ('395 Patent FH, 7/14/2008 Resp. to OA and Amend. at 6-7) (emphasis in original); *see also* Ex. 11 (Holtz) at col. 27, lines 6-10. None of these statements limit the invention to only two-salt systems. Rather, each makes clear that Amgen distinguished Holtz in both the prosecution of the parent application and the '707 Patent as not disclosing the particular salts of the then pending claims in those applications. Further, the prosecution of the parent application is not germane to the scope of the '707 Patent claims because the parent application claims are directed to "citrate and phosphate" subject matter that differs from the claims of the '707 Patent, as discussed below.

b. Because the Limitation Is Literally Met in Mylan's Process, Mylan's Motion Fails Regardless of the Merits of Amgen's Allegations That the Limitation Is Met Equivalently

Mylan's Motion asserts that prosecution history estoppel and the dedication-disclosure doctrine bar Amgen's alternative argument that this limitation is met under the doctrine of

equivalents because Mylan uses an [redacted]. Mylan Br. at 17-19. This misses the point. Amgen has undeniably alleged that the salt pair limitation is met literally based on the [redacted], which must be credited as true and is more than sufficient to show a plausible claim for relief. Amgen's allegations show that the limitation is literally met in Mylan's process, regardless of the merits of Amgen's alternative argument that the limitation is met under the doctrine of equivalents.

In any event, Mylan is wrong that prosecution history estoppel bars application of doctrine of equivalents as to the salt pair limitation. [redacted]. Ex. 1 (Amgen's (3)(C) Statement) at 34-35; [redacted] have different lyotropic values and, as a combination, are insubstantially different from one or more of the salt pairs claimed in the '707 Patent as to the ability to increase the dynamic capacity of a HIC column for a protein. Ex. 1 (Amgen's (3)(C) Statement) at 35; Ex. 2 (Amgen's Contentions) at Appx. A 2-4, 5-7. At the very least, factual disputes remain as to whether [redacted] are equivalent to one of the claimed combinations in achieving increased dynamic capacity [redacted]. It is thus premature at this early stage, before the completion of fact discovery and without expert discovery, to resolve this question of infringement under the doctrine of equivalents, a question that the Federal Circuit has cautioned "rarely come[s] clear on a premature record." *Mylan Institutional LLC v. Aurobindo Pharma Ltd.*, 857 F.3d 858, 866 (Fed. Cir. 2017) (quoting *Jeneric/Pentron, Inc. v. Dillon Co.*, 205 F.3d 1377, 1384 (Fed. Cir. 2000)).

Amgen did not make a clear and unmistakable disavowal of "more salts than the two-salt system" as Mylan asserts here. Mylan Br. at 21. Courts "do not presume a patentee's arguments

to surrender an entire field of equivalents through simple arguments and explanations to the patent examiner." *Conoco Inc. v. Energy & Env. Int'l, L.C.,* 460 F.3d 1349, 1364 (Fed. Cir. 2006). While a patentee may surrender a possible equivalent found in the prior art by argument during prosecution, that does not equate to a surrender of other possible equivalents. *See id.* Here, Amgen distinguished Holtz in the '707 Patent prosecution as not disclosing enhancing the dynamic capacity of the HIC column because Holtz applied a "single salt." Ex. 5 at 55 ('707 Patent FH, 8/22/2011 Reply to OA at 6). In response to an obviousness rejection over Holtz, the applicants asserted that "to the extent Holtz et al applied a salt in a HIC operation, it was as single salt and it was used in a traditional and well-established capacity"; the use of a "single salt" will not enhance the dynamic capacity of a HIC column as required in the '707 Patent claims. *Id.* Nothing in these statements is a disavowal of more salts than the two-salt system.

Further, Amgen distinguished Holtz in the '707 Patent prosecution on the grounds that it "does not disclose, suggest, or contemplate any steps involving a combination of two salts for any purpose whatsoever" and that it failed to teach any combination of salts that increases the "dynamic capacity of a HIC." Ex. 5 at 54 ('707 Patent FH, 8/22/2011 Resp. to OA at 5); *id.* at 6-7 ('707 Patent File History, 1/26/2011 Resp. to OA at 5-6). These statements do not clearly and unmistakably surrender all salts other than those in the claims; they simply make clear that the particular process in Holtz—using a combination of salts that was not reported to increase dynamic capacity—is not within the scope of the claims. *See Conoco, Inc.*, 460 F.3d at 1364.

Recognizing that there is no estoppel from the '707 Patent prosecution, Mylan relies exclusively on statements that Amgen made during prosecution of the parent application (for U.S. Patent No. 7,781,395 ("the '395 Patent") (D.I. 80-6)). But the salt pair limitation of the parent application claims is "citrate and phosphate" and thus not the same subject matter of the

'707 Patent claims (despite Mylan's assertion otherwise, *see* Mylan Br. at 22). *See* D.I. 80-6 ('395 Patent) at claim 1. Rather than reciting a "citrate and phosphate" salt pair, the '707 Patent claims require that "the first and second salts are selected from the group consisting of citrate and sulfate, citrate and acetate, and sulfate and acetate." Thus, Amgen's statements in the parent application prosecution do not limit the claims of the '707 Patent. *See Invitrogen Corp.*, 429 F.3d at 1078 ("[T]he prosecution of one claim term in a parent application will generally not limit different claim language in a continuation application"); *Biogen, Inc.*, 318 F.3d at 1141 ("When the applicant is seeking different claims in a divisional application, estoppel generally does not arise from the prosecution of the parent.").

Additionally, Mylan argues that Amgen cannot assert infringement under the doctrine of equivalents with respect to [redacted] because Amgen disclosed but did not claim [redacted] in the '707 Patent. Mylan Br. at 19. This too fails. For the dedication-disclosure doctrine to apply, the "unclaimed subject matter must have been identified by the patentee as an alternative to a claim limitation" and "the disclosure must be of such specificity that one of ordinary skill in the art could identify the subject matter that had been disclosed and not claimed." *SanDisk Corp. v. Kingston Tech. Co., Inc.*, 695 F.3d 1348, 1363-64 (Fed. Cir. 2012). Not "any generic reference in a written specification necessarily dedicates all members of that particular genus to the public." *Id.* (quoting *PSC Comput. Prods. v. Foxconn Int'l, Inc.*, 355 F.3d 1353, 1360 (Fed. Cir. 2004)).

Here, Mylan asserts that col. 4, lines 33-46 of the '707 Patent "discloses (but does not claim)" a list of salts [redacted] Mylan Br. at 6. But that is simply a list of lyotropic series which identifies [redacted]. *See* '707 Patent. at col. 4, lines 33-46; col. 5, lines 5-10. That portion of the patent does not make any

statement about the salt, [redacted], let alone whether it is covered by the claims. Mylan also relies on column 3, lines 22 to 24 of the '707 Patent (D.I. 81-2) to assert that "Amgen disclosed the use of [redacted] 'as useful for purifying proteins using HIC columns' yet failed to claim [redacted] in any of the listed salt pairs." Mylan Br. at 19. But that part of the patent describes [redacted] in the context of explaining the prior art; it is not a disclosure of [redacted] as used in the claimed invention. [redacted]

[redacted] Nor does this paragraph disclaim the use of [redacted] as a salt in the invention. It simply notes the use of [redacted] in the prior art, and contrasts that with the claimed invention of increasing the dynamic capacity of a column for a protein using a first salt and a second salt where each salt is present at a lower concentration than the concentration taught in the prior art for a single-salt HIC system.

In addition, Mylan argues that "Amgen was forced to narrow its claims in the parent application to a combination of citrate and phosphate and failed to claim [redacted], thus dedicating it to the public, twice." Mylan Br. at 19. This is incorrect. Amgen did not identify [redacted] "as an alternative to a claim limitation" in the parent application claims, as would be required for subject matter to be dedicated to the public. *See SanDisk Corp.*, 695 F.3d at 1363-64. Rather, the Patent Office Examiner issued a restriction requirement in the parent application, which is used when the application claims two or more independent and distinct inventions. Ex. 7 at 54-56 ('395 Patent FH, 12/10/2006 Detailed Action at 2-4)); *see Pfizer, Inc.*

v. Lee, 811 F.3d 466, 469 (Fed. Cir. 2016); *see also Bayer Aktiengesellschaft v. Duphar Int'l Research B.V.*, 738 F.2d 1237, 1243 (Fed. Cir.1984) ("[L]imiting the claims because of a restriction requirement, as occurred here, would not necessarily invoke file history estoppel.). In response, Amgen amended the claims to recite only citrate and phosphate salts. Ex. 8 at 4 ('395 Patent FH, 4/13/2007 Resp. to Rest. Req. at 2); *id.* at 44 ('395 Patent FH, 11/16/2007 Resp. to OA at 3). This amendment does not dedicate the use of [redacted] to the public for the parent claims, let alone the '707 Patent claims which are directed to different "citrate and phosphate" subject matter.

Finally, Mylan argues that because Amgen "repeatedly" distinguished the prior art based on the particular combination of salts, Amgen has indicated to competitors that it surrendered processes using combinations of salts different from the salt pairs recited in the claims. Mylan Br. at 18-19. This ignores the fact that Mylan's process uses [redacted] Further, Amgen's statements to the Patent Office make clear that the prior art does not disclose particular "combinations of salts that *increase the dynamic capacity*" of the HIC column as is required by the '707 Patent claims. Ex. 5 at 6 (1/26/2011 Response to OA at 5) (emphasis in original). Those statements do not unmistakably surrender all salt pairs except those that are claimed.

3. Mylan's Manufacturing Process Meets the Salt Concentration Limitation, as Amgen Has Alleged

Amgen alleges that the concentration of salts used in Mylan's process is equivalent to the claimed concentrations. D.I. 1 ¶ 90; Ex. 1 (Amgen's (3)(C) Statement) at 37-38. As Amgen's 3(C) Statement asserts:

> Claim 1 discloses a concentration range of between about 0.1 M to 1.0 M of each salt in the mixture. [redacted]

[redacted]

Ex. 1 (Amgen's (3)(C) Statement) at 37-38. These allegations must be credited as true and thus Amgen has made a more than plausible claim that this limitation is met equivalently.

Mylan argues that there is no infringement because its salt concentrations do not fall within the scope of "about 0.1 M." Mylan Br. at 23 ("No plausible construction of 'about 0.1 M' could stretch the lower boundary of the claimed concentration range [redacted]."). But the term "about 0.1 M" will be the subject of claim construction and discovery, as its meaning is informed by evidence as to how one of ordinary skill in the art would understand that term. The interpretation of that term cannot be resolved now, on a motion for judgment on the pleadings. As with the other claim construction disputes Mylan raises in its Brief, these are "classic *Markman*" arguments that are not suitable for resolution on a motion for judgment on the pleadings. *See Nalco Co.*, 883 F.3d at 1349. Moreover, Mylan's claim construction arguments are misplaced because the only assertion tested by Mylan's motion is Mylan's infringement of this element under the doctrine of equivalents. *See* Ex. 1 (Amgen's (3)(C) Statement) at 37-38.

In addition, Mylan incorrectly argues that Amgen surrendered salt concentrations lower than 0.1 M. Mylan Br. at 23-24. Here again, the sole basis for Mylan's argument are statements in the parent application which are directed to the concentration of a different pair of salts than the salt pairs claimed in the '707 Patent. As above, these statements do not bar Amgen from asserting infringement under the doctrine of equivalents as to the '707 Patent. The Patent Office Examiner issued a restriction requirement to the parent application, which is used when the

application claims two or more independent and distinct inventions. *See Pfizer, Inc. v. Lee*, 811 at 469. In response, Amgen amended the claims to recite only citrate and phosphate salts. Amgen then added in the parent application a concentration limitation for claims directed to "citrate and phosphate salts"; this amendment was a preliminary amendment that was not made in response to a prior art rejection. Ex. 8 at 4-5 ('395 Patent FH, 4/13/2007 Resp. to Restriction Requirement at 2-3); *id.* at 45 ('395 Patent FH, 11/16/2007 Resp. to OA at 3). Indeed, Mylan does not argue that this amendment leads to prosecution history estoppel. Mylan Br. at 23.

Amgen's statements in the parent application as to concentration are not an estoppel as to the concentration of the salt pairs claimed in the '707 Patent because the parent application statements are limited to the concentration of "citrate and phosphate" salts; nothing in the parent application addresses the concentration of the different salt pairs claimed in the '707 Patent which are "citrate and sulfate, citrate and acetate, and sulfate and acetate." *Compare* D.I. 81-2 ('707 Patent) at claims 1 and 10 *with* D.I. 81-6 ('395 Patent) at claim 1. The specification teaches that different salts and different salt combinations have different effectiveness for precipitation of proteins from aqueous solutions; indeed, the patent identifies and ranks the cations and anions based on their "salting out" and "salting-in" effect on proteins. D.I. 81-2 ('707 Patent) at col. 4, lines 42-51 ("combining two different salts having different lyotrophic values with a protein preparation allows more protein to be loaded onto a column with no or negligible breakthrough compared with higher salt concentrations of each single salt"). Therefore, any discussion of the concentrations of the "citrate and phosphate" salt pair in the parent application is not meaningful to the concentration of the different salt pairs claimed in the '707 Patent.

Even if the Court were to look to the prosecution of the parent application, the applicant's statements are not an estoppel as to concentration of the salt pairs claimed in the '707 Patent, particularly in view of the applicant's later statements in the '707 Patent application. In the parent application, Amgen distinguished "citrate and phosphate salts" claims over Holtz on a combination of grounds, including that Holtz did not teach combining the protein with the particular combination of "citrate and phosphate salts" at the particular 0.1 M and 1.0 M concentration in the parent application claims. Ex. 9 at 7-8 ('395 Patent FH, 7/14/2008 Resp. to OA and Amend. at 6-7). This does not give rise to an estoppel because the prior art was distinguished based on a combination of various grounds (the concentration of a particular salt pair), and not specifically the concentration of any salt pairs. Mylan concedes that arguments based on a combination of grounds do not give rise to an estoppel. *See* Mylan Br. at 21 n.9 ("'[W]here a patent applicant sets forth multiple bases to distinguish between its invention and the cited prior art, the separate arguments [can] create separate estoppels as long as the prior art was not distinguished based on a combination of these various grounds.' *PODS, Inc. v. Porta Stor, Inc.*, 484 F.3d 1359, 1367 (Fed. Cir. 2007) (internal quotation marks and citation omitted)."); *see also Biogen, Inc.*, 318 F.3d at 1141 ("Every statement made by a patentee during prosecution to distinguish a prior art reference does not create a separate estoppel. Arguments must be viewed in context.") (quoting *Read Corp. v. Portec, Inc.*, 970 F.2d 816, 824 (Fed. Cir. 1992) *abrogated on unrelated grounds by Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996)). Thus, nowhere in the parent application did Amgen surrender claim scope with respect to the concentration of the specific salt pairs in the particular claims at issue here, and especially the [redacted] that is used in the Mylan process.

Tellingly, when the '707 Patent claims were rejected over the same Holtz prior art, Amgen did not distinguish the claims based on the concentration of the claimed salt pairs of "citrate and sulfate, citrate and acetate, and sulfate and acetate." Ex. 5 at 53-56 ('707 Patent FH, 8/22/2011 Reply to OA at 4-7). Indeed, Amgen did not challenge the Patent Office's position that Holtz discloses the use of a concentration that squarely overlaps with the "0.1 M and 1.0 [M]" concentration claimed in the '707 Patent. The Patent Office said that Holtz discloses "a number of salts between 0.2 M and 2.0M concentration, ***preferably between 0.4 and 1 M concentration***." Ex. 5 at 6 (1/26/2011 Response to OA at 5) (emphasis added); Ex. 4 at 23 (10/07/2010 Detailed Action at 4). Amgen then acknowledged the Patent Office's position and distinguished Holtz on the ground that it did not recite the particular combination of salts claimed in the '707 Patent. Ex. 5 at 6-7 (1/26/2011 Response to OA at 5-6). Further, given that the '707 Patent prosecution statements came after the applicant's statements in the parent application, they cannot be ignored. No competitor reading these prosecution histories would reasonably believe that Amgen had surrendered concentration subject matter with respect to the particular salt pairs in the '707 Patent claims. *Conoco,* 460 F.3d at 1364; Mylan Br. at 18.

In addition, Amgen later asserted that Holtz applied a single salt, and that the use of a single salt does not disclose enhancing the dynamic capacity of a HIC column as required of the claims. Ex. 5 at 54-55 ('707 Patent FH, 8/22/2011 Reply to OA at 5-6). Nowhere did Amgen assert that the '707 Patent's claim to concentrations of the claimed salt pairs distinguished those claims over the prior art. Therefore, neither Amgen's statements in the parent application nor its statements in the '707 Patent prosecution are an estoppel or disclaimer of lower concentrations of the claimed "citrate and sulfate, citrate and acetate, and sulfate and acetate" salt pairs.

In addition, the Court cannot resolve as a matter of law that the concentration of "citrate and sulfate, citrate and acetate, and sulfate and acetate" is the same as or has the same function, way, and result as the concentration of other salt pairs as claimed in the '707 Patent. Whether the concentration of Mylan's salts is equivalent to the salt concentration claimed in the '707 Patent is a disputed factual issue, particularly as Amgen expects there will be discovery on the concentrations of salts in Mylan's process and their ability to increase the dynamic capacity of a HIC column. At the very least, it is premature to resolve this question of infringement under the doctrine of equivalents at this early stage before completion of fact discovery and before expert discovery even begins. *See Mylan Institutional LLC*, 857 F.3d at 866.

Mylan also argues that Amgen's statements in an opposition as to a European patent is an "admission" of disclaimer of lower concentration of salts. Mylan Br. at 23 n.12. This is incorrect. Amgen's statements were not made for the '707 Patent application and they are not admissions because representations to foreign patent offices do not establish "foreign prosecution estoppel." *See Tanabe Seiyaku Co., Ltd. v. U.S. Int'l Trade Comm'n*, 108 F.3d 726, 733 (Fed. Cir. 1997). Indeed, statements made during prosecution of foreign counterparts in response to patentability requirements unique to foreign law are irrelevant to claim construction of U.S. patents. *Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, 457 F.3d 1284, 1290 (Fed. Cir. 2006); *see AIA Eng'g Ltd. v. Magotteaux Int'l S/A*, 657 F.3d 1264, 1279 (Fed. Cir 2011).

B. The Delaware Court's Decision in *Coherus* Does Not Compel This Court to Grant Mylan's Motion

Amgen Inc. v. Coherus Biosciences Inc. addressed only whether Coherus's manufacturing process—which is confidential and presumably different from Mylan's manufacturing process—meets the salt pair limitation under the doctrine of equivalents. No. 17-546-LPS-CJB, 2018 WL 1517689 at *1 (D. Del. March 26, 2018). That decision did not address whether the salt pair

limitation is literally met or whether the salt concentration limitation is met. *Id.* at *2-3. As the Delaware court noted, it did not consider Coherus's argument that it cannot infringe because its manufacturing process does not use a salt pair at the required concentration. *Id.* at *3 n.4. Thus, the *Coherus* decision does not control the outcome here.

Further, infringement "requires determination on its own facts." *Del Mar Avionics, Inc. v. Quinton Inst. Co.*, 836 F.2d 1320, 1324 (Fed. Cir. 1987); *Pfaff v. Wells Elects., Inc.*, 5 F.3d 514, 519-20 (Fed. Cir. 1993) (finding of prosecution history estoppel in one case does not preclude infringement finding under the doctrine of equivalents for a different device or process in a later case as to the same patent). Here, Coherus is a different biosimilar company than Mylan. Coherus has its own confidential manufacturing process for its own proposed biosimilar product. The Delaware district court's decision does not compel granting Mylan's motion here at least because Mylan's process must be inferred to differ from Coherus's process. Mylan uses [redacted] whereas only an assertion of equivalence with respect to this claim limitation was considered by the Delaware court. Ex. 1 (Amgen's (3)(C) Statement) at 34-35. Thus, the reasonable inference to be drawn from the facts before the Court is that the relevant facts for infringement here are different than the facts at issue in the *Coherus* action. In recognition of these differences, Amgen asserts in this case that Mylan's manufacturing process literally infringes the claimed combination of salt pairs, which is a theory that Amgen did not advance as to Coherus's manufacturing process in Delaware. *See id.*; *Coherus*, 2018 WL 1517689 at *4. *Coherus* does not and cannot resolve the issues here.

III. CONCLUSION

For the foregoing reasons, Amgen respectfully requests that the Court deny Mylan's Motion.

Respectfully submitted,

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Dated: April 27, 2018

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CERTIFICATE OF SERVICE

I hereby certify that on the 27th day of April, 2018, I electronically filed the foregoing **AMGEN'S RESPONSE IN OPPOSITION TO MYLAN'S MOTION FOR JUDGMENT ON THE PLEADINGS PURSUANT TO RULE 12(c) REGARDING U.S. PATENT NO. 8,273,707** via email, on Defendants Mylan Inc., Mylan Pharmaceuticals Inc., Mylan GmbH, and Mylan N.V.'s counsel of record, as follows:

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