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

AMGEN INC., et al.,	)	
	)	
Plaintiffs,	)	
	)	2:17-cv-01235
v.	)	
	)	
MYLAN INC., et al.,	)	
	)	
Defendants.	)	

OPINION

Mark R. Hornak, United States District Judge

Amgen, Inc. ("Amgen") alleges that Mylan, Inc. ("Mylan") infringes two of its patents: U.S. Patent No. 9,643,997 (the "'997 Patent") and U.S. Patent No. 8,273,707 (the "'707 Patent"). The parties dispute multiple claim terms in both patents. The parties have submitted proposed constructions for the terms and the matter has been fully briefed. (ECF Nos. 100, 106, 110, 114, 130, 132). The Court heard argument on the parties' positions on September 21, 2018 and the matter is now ripe for disposition.

I. BACKGROUND

Amgen produces Neulasta® and a family of related FDA-approved pharmaceuticals that are used to prevent infection in cancer patients receiving immunosuppressive anti-cancer drugs. The active ingredient in some of these pharmaceutical products is pegfilgrastim, a modified form of the protein filgrastim. Filgrastim itself is a modified form of the naturally occurring glycoprotein granulocyte-colony stimulating factor ("G-CSF"). G-CSF stimulates the production of certain white blood cells known as neutrophils. These cells are an essential component of the

human immune response to pathogens. Patients undergoing chemotherapy for the treatment of cancer commonly experience a reduction of their white blood cell count as a side effect of the treatment. This condition—neutropenia—leaves these patients particularly susceptible to life-threatening infections. By stimulating the production of neutrophils, G-CSF can reduce the risk of these infections.

Filgrastim, the precursor to pegfilgrastim, is conventionally produced by inserting the gene (*i.e.*, the DNA) that encodes G-CSF into a bacterial cell. These cells are then grown on an industrial scale and are stimulated to begin producing the protein through the cells' natural mechanisms. Though these micro protein "factories" can work scientific wonders, they can also make mistakes. The desired protein is often produced along with other native bacterial proteins, and these cellular products aggregate in insoluble or semi-soluble inclusion bodies within the cells. The desired proteins are also often misfolded during their synthesis, rendering them ineffective. Accordingly, the produced filgrastim must be further isolated and purified before it can be utilized as a pharmaceutical product.

The patents in suit are both generally directed to these protein purification techniques. The following simplified description of these processes is provided for background purposes only. Additional technical detail will be provided in context of the individual patents. In simplified terms, proteins are three-dimensional biological structures that are composed of chains of individual units called amino acids. To obtain their functional three-dimensional shape, chains of amino acids fold up on themselves. The target proteins that the genetically modified bacteria produce are often misfolded and tangled up with other proteins and other cellular debris within the bacterial cells themselves. These masses are known as "inclusion bodies," and are roughly akin to balls of yarn with the target proteins interspersed within. The bacterial cells must first be

broken open, or "lysed," to obtain these inclusion bodies. Chemicals are then applied to "solubilize," or dissolve, the components of the inclusion bodies, including the target proteins. Continuing the yarn ball analogy, this step would be like untangling the threads of yarn making up the yarn ball. At this point, the target proteins are unfolded chains of amino acids, as if they were straightened-out threads of yarn.

Other chemicals are then added to the solution that cause the protein to "refold" into its active, functional three-dimensional shape. However, the proteins themselves are still in solution, now known as a "refold solution," with other proteins from the inclusion bodies, cellular debris, and other contaminants. The targeted threads of the yarn ball have been folded (or "knotted into") their desired shape, but the rest of the yarn ball is still floating around with them. These other components must be removed, and this is accomplished by taking advantage of regions of the target proteins that have affinities for materials with certain chemical properties.

Column chromatography is a common technique that is employed for this purification step. In simplified terms, a column is packed with a "separation matrix," which is often a solid resin that contains regions that chemically attract regions of the target proteins. Solutions may be introduced into the top of the column and flow downward, contact the separation matrix, and flow out of the column. As the refold solution flows past the separation matrix, the proteins "stick" to the matrix as the rest of the refold solution—which contains the contaminants and other materials—flows out of the column to be collected and discarded. Some of the contaminants will nonetheless stick to the separation matrix. Thus, a "washing buffer" is applied, which is designed to wash away the remaining contaminants as it flows out of the column while preserving the attractive forces between the target proteins and the separation matrix. At this point, ideally, only the targeted proteins remain stuck to the separation matrix. An "elution"

solution is then applied to the separation matrix. This solution is designed to "un-stick" the target proteins from the separation matrix and carry the target proteins out of the column. As this solution flows out of the column, it is collected. This collected solution is the "elution pool," and ideally it will contain the functional, correctly folded, target proteins without the contaminants. Additional purification steps may be needed before the targeted proteins are suitably pure for therapeutic use.

The '997 Patent, entitled "Capture Purification Processes for Proteins Expressed in a Non-Mammalian System" issued on May 9, 2017. The '707 Patent, entitled "Process for Purifying Proteins" issued on September 25, 2012. Amgen was the applicant, and is the current assignee, of both patents.

Mylan produces generic versions of brand-name pharmaceuticals. Amgen accuses Mylan of seeking FDA approval for a biosimilar version of the active ingredient in the Neulasta® family of products, pegfilgrastim. The parties' current dispute centers around Mylan's allegedly infringing purification processes. Mylan argues that its purification processes do not infringe the claims of Amgen's asserted patents and has moved for a judgment on the pleadings pursuant to Fed. R. Civ. P. 12(c). (ECF No. 79).[1] The parties have proposed five terms in the '997 Patent and four terms in the '707 Patent for construction.[2]

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[1] In the briefing directed to the Motion for Judgment of the Pleadings, both parties advanced arguments related to the construction of disputed terms of the '707 Patent. (ECF Nos. 80, 81, 86, 87, 95, 97). The resolution of these claim construction disputes could be, in the Court's estimation, dispositive of several considerations in that Motion. The Court thus determined that resolution of the Motion was inappropriate prior to the Court's construction of the disputed claim terms, and therefore dismissed the Motion without prejudice and subject to its reassertion following the Court's construction of the disputed terms. (ECF No. 170).

[2] The parties had previously disputed an additional term in the '707 Patent but have since entered into a joint stipulation regarding the construction of that specific term. (ECF Nos. 158, 161). The Court, having concluded that the parties' joint position with respect to the jointly proposed construction was supported by the intrinsic evidence, approved and adopted the parties' joint stipulation. (ECF No. 162).

II. LEGAL STANDARD

Claim construction is a matter of law that is to be exclusively determined by the Court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 384 (1996). A district court must construe a claim term when the parties present a "fundamental dispute regarding the scope" of the term. *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co., Ltd.*, 521 F.3d 1351, 1361–63 (Fed. Cir. 2008). The purpose of claim construction is to "give meaning to the limitations actually contained in the claims" and not to "obviate factual questions of infringement and validity" by redefining claim language or reading in limitations. *Am. Piledriving Equip. Inc. v. Geoquip, Inc.*, 637 F.3d 1324, 1331 (Fed. Cir. 2011). But, though claim construction should not "obviate" factual determinations related to infringement or validity, claim construction is always the first step of any infringement or validity contention. *See State Contracting & Eng'g Corp. v. Condotte Am., Inc.*, 346 F.3d 1057, 1068 (Fed. Cir. 2003).

Claim construction begins with an analysis of the claims themselves and their language. *Scanner Techs. Corp. v. ICOS Vision Sys. Corp.*, 365 F.3d 1299, 1303 (Fed. Cir. 2004). The words of a claim "are generally given their ordinary and customary meaning" which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of invention." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (*en banc*). But claim terms "must be construed in light of the specification and prosecution history, and cannot be considered in isolation." *GE Lighting Solutions, LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1308–09 (Fed. Cir. 2014) (citing *Phillips*, 415 F.3d at 1313). That is, "the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313. At times, the ordinary meaning of the claim terms is so apparent that

detailed construction and analysis is unnecessary. *Id.* at 1314. But, more often, this meaning is "not immediately apparent" and thus courts "look[] to the sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean." *Id.* (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004)).

"The specification is the single best guide to the meaning of a disputed claim term and is, thus, the primary basis for construing the claims." *Trustees of Columbia Univ. in City of N.Y. v. Symantec Corp.*, 811 F.3d 1359, 1362 (Fed. Cir. 2016) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996); *Phillips*, 415 F.3d at 1315) (internal quotation marks omitted). But, limitations from the specification are generally not to be read into the claims. *See, e.g., Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1186 (Fed. Cir. 1998); *Intel Corp. v. U.S. Int'l Trade Comm'n*, 946 F.2d 821, 836 (Fed. Cir. 1991) ("[W]here a specification does not *require* a limitation, that limitation should not be read from the specification into the claims.") (emphasis in original). And, though a specification will often describe particular and specific embodiments of an invention, claims should generally not be construed to be limited to those embodiments. *See Nazomi Commc'ns, Inc. v. ARM Holdings, PLC*, 403 F.3d 1364, 1369 (Fed. Cir. 2005).

Finally, courts may consider extrinsic evidence, such as expert testimony, dictionaries, and treatises, but "such evidence is generally of less significance than the intrinsic record." *VirnetX, Inc. v. Cisco Sys., Inc.*, 767 F.3d 1308, 1316 (Fed. Cir. 2014) (citing *Phillips*, 415 F.3d at 1317). Further, this extrinsic evidence cannot be "used to contradict claim meaning that is unambiguous in light of the intrinsic evidence." *Phillips*, 415 F.3d at 1324.

III. DISCUSSION

The '997 Patent

The '997 Patent is entitled "Capture Purification Processes for Proteins Expressed in a Non-Mammalian System" and issued on May 9, 2017. Amgen was the applicant for the patent and the current assignee. The '997 Patent generally discloses a simplified protein purification process.'997 Patent at 1:56–60. Non-mammalian cells, such as microbial cells, can be genetically engineered to produce proteins. *Id.* at 3:65–67. These organisms will typically deposit the proteins in large insoluble aggregates called inclusion bodies. *Id.* at 4:1–3. The expressed proteins in these inclusion bodies are typically unfolded or misfolded, and thus not therapeutically useful. *Id.* at 12:27–32. Accordingly, the proteins must be isolated from the cells that produce them, purified, and refolded into their correct three-dimensional configuration before they are viable for use as a pharmaceutical product or precursor. *Id.*

The '997 Patent teaches such a purification process that is purportedly more efficient than processes that were known in the art. In one embodiment, the microbial cells are stimulated to produce, or express, the proteins of interest. '997 Patent at 13:9–20. These cells are then lysed to break apart the cells and release the target proteins of interest (often entangled in inclusion bodies). *Id.* at 13:33–36. The protein is then separated from the lysis pool by employing conventional methods, such as centrifugation, to isolate the protein of interest. *Id.* at 13:48–56. The expressed protein is then solubilized in solubilization solution. *Id.* at 13:65–14:3. The function of the solubilization solution is to solubilize and denature the expressed protein so that it can be later refolded into a suitable configuration. *Id.* This refolding is accomplished by forming a refold solution, which comprises the solubilization solution, solubilized protein, and a refold buffer that is chosen, based on the protein of interest, to shift the thermodynamics of the solution

to encourage proper protein folding. *Id.* at 14:27–40. The refold solution is then applied to a separation matrix. *Id.* at 15:23–30. The expressed protein interacts with the separation matrix, and then a wash buffer is applied to the matrix to preserve these interactions and to wash away contaminants and other impurities from the separation matrix. *Id.* at 16:1–4. The target protein is then eluted from the separation matrix by applying an elution solution, which promotes the release of the protein from the separation matrix. *Id.* at 16:19–23. In contrast to prior art methods, the '997 Patent teaches that the refold solution can be applied directly to the separation matrix without intervening steps such as dilution of the refold solution or removing other components of the refold solution that may reduce the ability of the expressed protein to associate with the separation matrix. *Id.* at 15:50–67. According to the '997 Patent, this results in a more efficient process that conserves time and resources. *Id.*

A patent in the same family as the '997 Patent was construed in the Northern District of California by Judge Seeborg in *Amgen Inc. v. Sandoz Inc.*, No. 14-cv-04741, 2016 WL 4137563 (N.D. Cal. Aug. 4, 2016). (construing U.S. Patent No. 8,940,878 (the "'878 Patent")). The '878 Patent shares a specification with the '997 Patent that is identical in all material aspects. The *Sandoz* court construed two of the five terms disputed in this case, and also construed a term that is nearly identical to one of the terms disputed in this case. Mylan asks this Court to adopt the constructions of the *Sandoz* court of each such claim. Mylan offers several arguments as to why Amgen should be precluded from challenging the constructions of the *Sandoz* court, namely, that Amgen was a party to the previous action, that Amgen failed to appeal adverse constructions, and that Amgen should not be allowed to now assert that certain terms require a construction when they did not so assert in *Sandoz*. While the Court is mindful of the importance of

uniformity in patent claim term interpretation, *see Markman*, 517 U.S. at 390, the Court does not agree with Mylan's arguments.

A. Amgen is not collaterally estopped from asserting the claim construction arguments that they present in this case.

The Federal Circuit applies the law of the regional circuit in determining whether collateral estoppel applies to another district court's claim construction. *See RF Del., Inc. v. Pac. Keystone Techs., Inc.*, 326 F.3d 1255, 1261 (Fed. Cir. 2003). Under Third Circuit law, in order for collateral estoppel to apply, a party must demonstrate that "(1) the identical issue was previously adjudicated; (2) the issue was actually litigated; (3) the previous determination was necessary to the decision; and (4) the party being precluded from relitigating the issue was fully represented in the prior action." *Jean Alexander Cosmetics, Inc. v. L'Oreal USA, Inc.*, 458 F.3d 244, 249 (3d Cir. 2006) (internal quotations omitted). The Third Circuit also considers whether the party being precluded "had a full and fair opportunity to litigate the issue in question in the prior action" and "whether the issue was determined by a final and valid judgment." *Id.* (quoting *Sebrowski v. Pittsburgh Press Co.*, 188 F.3d 163, 169 (3d Cir. 1999); *Nat'l R.R. Passenger Corp. v. Pa. Pub. Utility Comm'n*, 288 F.3d 519, 525 (3d Cir. 2002)).

Following the Northern District of California's *Markman* claim construction Order, the defendant Sandoz moved for, and was granted, summary judgment of non-infringement. *Amgen Inc. v. Sandoz Inc.*, 295 F. Supp. 3d 1062, 1071 (N.D. Cal. 2017). Amgen filed an appeal with the Court of Appeals for the Federal Circuit on February 12, 2018, currently pending on the Federal Circuit's docket as No. 18-1551. Amgen appealed the construction of the "washing" and "eluting" elements of Claim 7 of the '878 Patent, (Amgen Appeal Br. at 3, ECF No. 111-12), because these terms were essential to the *Sandoz* court's grant of summary judgment. Mylan contends that Amgen's decision to only appeal these claim construction rulings from the *Sandoz*

order effectively operates as a waiver of any claim construction arguments that Amgen now advances as to non-appealed constructions.

As a preliminary matter, the claim construction rulings that Amgen appealed are not final judgments and are thus not preclusive in this Court. *See Phil-Insul Corp. v. Airlite Plastics Co.*, 854 F.3d 1344, 1357–58 (Fed. Cir. 2017) (explaining that "the claim constructions became final *when we affirmed them on appeal.*") (emphasis added). By implication, claim constructions that are subject to a pending appeal are not final.[3] For this reason, *see Nat'l R.R. Passenger Corp.*, 288 F.3d at 525, the Court will treat the *Sandoz* court's constructions of the "washing" and "eluting" terms as persuasive, but not binding, authority.

B. Amgen is not precluded from asserting, nor has it waived, arguments relating to the construction of "under conditions suitable for the protein to associate with the matrix."

The Court concludes that Amgen's "decision" to not appeal the construction of "under conditions suitable for the protein to associate with the matrix" is also not preclusive, nor does it operate as a waiver, because this construction was not "necessary to" the summary judgment decision. *See L'Oreal*, 458 F.3d at 239. The final judgment in the *Sandoz* case was grounded in the determination that the washing and eluting steps must be distinct and sequential in the process claimed by the '878 Patent, and that Sandoz's accused process did not meet these limitations. *Sandoz*, 295 F. Supp. 3d at 1069. And, at any rate, Amgen *could not have* appealed this construction because, as discussed, it was not necessary to the *Sandoz* court's summary judgment decision. *See Personalized User Model, LLP v. Google Inc.*, 797 F.3d 1341, 1350 (Fed.

[3] Mylan cites to *Nestle USA, Inc. v. Steuben Foods, Inc.*, 884 F.3d 1350 (Fed. Cir. 2018) and *Sightsound Techs, LLC v. Apple Inc.*, 809 F.3d 1307, 1316 (Fed. Cir. 2015) to assert that Amgen has waived its opportunity to argue for claim constructions contrary to what was construed by the *Sandoz* court. In the Court's estimation, these cases are inapposite because the *Sandoz* appeal is still pending. *Nestle* held that a party was estopped from raising arguments in an appeal after the Federal Circuit had *already rejected* those arguments in a related patent in an earlier appeal. *Nestle*, 884 F.3d at 1351–52. *Sightsound* dealt with the construction of two related patents in the same pending appeal. 809 F.3d at 1316. It makes sense that the Federal Circuit would want to decide the issues consistently within the same action.

Cir. 2015) (holding that the Federal Circuit lacked jurisdiction to review a district court's claim construction that did not affect the merits of the infringement controversy between the two parties in the appeal).

Mylan also cites *TM Patents, L.P. v. International Business Machines Corporation*, for the proposition that a party that "cuts off his right to review" a claim construction "cannot complain that the question was never reviewed on appeal" and that said construction remains preclusive. 72 F. Supp. 2d 370, 378 (S.D.N.Y. 1999). To the extent that this case is persuasive authority, the Court does not believe it governs the disposition of this matter. First, *TM Patents* dealt with a situation wherein a party to the previous action settled the case, and in this sense, chose to forego further review of the court's claim construction. *Id.* Here, several claim constructions from the *Sandoz* matter *have been* appealed, but by choosing to appeal these and not others, Amgen has not "cut off" its right to appellate review. As explained, this was not a true "choice" by Amgen, as it could not have appealed constructions that were not necessary to the *Sandoz* court's summary judgment decision. Second, *TM Patents* is not binding on this Court, and its conclusions and reasoning have been criticized by other district courts.[4] Finally, the Federal Circuit later ruled in *RF Delaware* that collateral estoppel did not apply in a case where another district court issued a claim construction order and that case settled prior to the court ruling on a pending summary judgment motion. 326 F.3d at 1260–61 ("We conclude that collateral estoppel does not apply in the present case because judgment, much less final judgment, was ever entered[.]"). This undercuts one of the *TM Patents* court's justifications for granting the prior court's claim construction order preclusive effect, and further calls into question whether *TM Patents* remains good law. *Cf. TM Patents*, 72 F. Supp. 2d at 379

[4] *See, e.g., Powervip, Inc. v. Static Control Components, Inc.*, No. 1:08-CV-382, 2011 WL 2669059, at *6 (W.D. Mich. July 6, 2011); *Kollmorgen Corp. v. Yaskawa Elec. Corp.*, 147 F. Supp. 2d 464, 467 (W.D. Va. 2001); *Graco Children's Prods., Inc. v. Regalo Int'l, LLC*, 77 F. Supp. 2d 660, 663 (E.D. Pa. 1999).

(concluding that claim construction orders were effectively "final" judgments such that collateral estoppel could apply).

As the Court sees it, Mylan is asking the Court to find that Amgen has "waived" any arguments for the construction of "under conditions suitable for the protein to associate with the matrix" based on another district court's construction of the term in a related (but different) patent in an unrelated infringement litigation. The final judgment in that case is currently on appeal, and Amgen could not have appealed this particular claim construction. The Court concludes that waiver is not appropriate here. This is not, as Mylan argues, giving Amgen a "second bite at the apple." (Mylan Br. at 10). While Amgen is proposing the same constructions before this Court as it advanced before the *Sandoz* court, 2016 WL 4137563 at *15–*16, the reality is that Amgen had not finished the first bite of the apple.

C. Amgen has not waived its opportunity to argue for the construction of certain claim terms based on its decision to not submit constructions for those terms in the *Sandoz* matter.

Neither party in the *Sandoz* matter sought a construction for the term "forming a refold solution comprising the solubilization solution and a refold buffer." And, in the *Sandoz* matter, Amgen did not identify the following terms for construction: "solubilization solution;" "separation matrix;"[5] and "buffer." Citing *Sage Products, Inc. v. Devon Industries, Inc.*, 126 F.3d 1420, 1423 (Fed. Cir. 1997), Mylan argues that Amgen cannot now argue that these terms require a construction in this case. (Mylan Resp. Br. at 10). In the Court's estimation, *Sage Products* does not provide support for the proposition that Mylan advances. That case appears to stand for the rather uncontroversial position that, absent some indication from the patentee to the contrary, the plain and ordinary meaning of claim terms control. *Sage Prods.*, 126 F.3d at 1423. And, that case was a direct appeal from a district court's judgment. The Federal Circuit held only

[5] This term is likewise not in dispute here.

that it would not review novel claim constructions *on appeal* that were not presented to the trial court. *Id.* at 1426. It did not hold that a party could not present constructions for terms that were not construed in an earlier, unrelated action in another district court. Further, there are different accused processes at issue here. In the *Sandoz* matter, the terms above were not in dispute and thus did not require a construction. As the Federal Circuit has stated:

> Claim construction is a matter of resolution of disputed meanings and technical scope, to clarify and when necessary to explain what the patentee covered by the claims, for use in the determination of infringement. It is not an obligatory exercise in redundancy.

U.S. Surgical Corp. v. Ethicon, Inc., 103 F.3d 1554, 1568 (Fed. Cir. 1997). The implication from this pronouncement is that neither litigants nor the courts are expected or required to identify claim terms for construction that are not in dispute or not material to an infringement determination. *See also O2 Micro*, 521 F.3d at 1362 ("[D]istrict courts are not (and should not be) required to construe *every* limitation present in a patent's asserted claims."); *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy."). Amgen is thus not precluded from seeking construction for these terms in this action. In light of a different accused process,[6] certain claim terms may now be material to the infringement determination where before they were not. Amgen is not prejudiced here for its not raising every possibly disputed claim term in the *Sandoz* case in light of all possibly infringing processes in a prior action involving only one such process.

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[6] Mylan suggests in its briefing that this would run afoul of the Federal Circuit pronouncement that claims are to be construed "without reference to the accused device." *See* Mylan Surreply Br. at 2, ECF No. 130 (citing *SRI Int'l v. Mitsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1118 (Fed. Cir. 1985)). This is incorrect. *SRI* teaches that the accused device is not to be considered or consulted when determining the meaning of the claims; it does not state that the accused device/process cannot influence the determination of what claims are material and/or disputed in a particular infringement determination. It appears plain to the Court that the specific features of a particular allegedly infringing product or process would set the contours of the disputes for litigation, including which claim terms are in dispute and require construction. The Court is aware of no rule of law that holds, or even suggests, that this is improper.

For the foregoing reasons, the Court will not treat the *Sandoz* court's claim constructions as binding and/or preclusive. The Court also holds that Amgen has not waived any arguments based upon its decision to not propose constructions for certain terms in the *Sandoz* action, or its decision to not appeal certain claim constructions from the *Sandoz* case. However, the Court recognizes the importance of uniformity in the interpretation of claim terms across related patents. *Nestle*, 884 F.3d at 1352; *see also Markman*, 517 U.S. at 390. Accordingly, the *Sandoz* court's claim construction order will be treated "as persuasive authority" and the Court will "provide [it] the deference provided any legal holding by a respected colleague." *See CoStar Realty Info., Inc. v. CIVIX-DDI, LLC*, No. 12 C 4968, 2013 U.S. Dist. LEXIS 135448, at *24 (N.D. Ill. Sept. 23, 2013).

1. "forming a refold solution comprising the solubilization solution and a refold buffer"

> **Amgen's Proposed Construction:** mixing the solution comprising the solubilized protein and one or more of a denaturant, a reductant, and a surfactant with a pH-buffered solution comprising one or more of a denaturant, an aggregation suppressor, a protein stabilizer, and a redox component providing the conditions for the protein to refold into its biologically active form
>
> **Mylan's Proposed Construction:** plain and ordinary meaning, no construction necessary

This disputed term appears in Step (b) of Claim 9 of the '997 Patent. The Court disagrees with Mylan's contention that construction of this term is not necessary because the scope of the term is fundamentally in dispute. *O2 Micro*, 521 F.3d at 1362–63. The fundamental disputes are the composition and identity of the solubilization solution, as well as the composition of the refold buffer. The scope of this claim may be substantially broader or narrower depending on how "the solubilization solution" and the "refold buffer" are defined. The breadth of these terms will likely be material to an infringement analysis.

a. Solubilization Solution

Parties disagree whether "the solubilization solution" in the disputed term refers to the solubilization solution that is formed in Step (a) of Claim 9.[7] Amgen, in its reply brief, recognizes that "a solubilization solution" in Step (a) provides the antecedent basis for "the solubilization solution" in Step (b). (Amgen Reply Br. at 12, ECF No. 114). The parties disagree about whether a strict identity of the two solutions is required. Amgen argues that additional components (notably, the "expressed protein" that is solubilized in the solution) may be added to the solubilization between Step (a) and Step (b), and also that certain components of the solution may be diluted or removed. In Amgen's view, because the "solubilization solution" is introduced in Step (a) as "*comprising one or more*" of a denaturant, reductant, and surfactant, '997 Patent at 22:39–43, as long as the solution continues to comprise *at least one* of those components, it is the "same" solubilization solution.

The Court does not agree and concludes that "the solubilization solution" in Step (b) of Claim 9 must refer to the same solubilization solution used to solubilize the protein in Step (a). First, the definite article "the" is used to introduce the solubilization solution in Step (b) of Claim 9, and "[s]ubsequent use of the definite article "the" or "said" in a claim refers back to the same term recited earlier in the claim." *Wi-LAN, Inc. v. Apple Inc.*, 811 F.3d 455, 462 (Fed. Cir. 2016). Amgen is correct, based on a plain reading of the claim, that Step (a) does not require that a "solubilization solution" that is utilized in that step must have all of the listed components. That is, any particular "solubilization solution" need only have one of a denaturant, reductant, or surfactant to be a "solubilization solution," and can also be comprised of any number of additional components. But once a particular solubilization solution is utilized in Step (a) to

[7] This step reads "(a) solubilizing the expressed protein in a solubilization solution comprising one or more of the following: (i) a denaturant; (ii) a reductant; and (iii) a surfactant; . . ." '997 Patent at 22:39–43.

solubilize the protein, any further introduction of "the solubilization solution" must necessarily refer to that *particular* solution that was utilized in Step (a) to solubilize the protein. If components were removed from a particular solubilization solution that was utilized in Step (a), it would no longer be the same solution being referred to in Step(b). The patentee chose to refer to "*the* solubilization solution" in subsequent recitations of the term, meaning that it must refer back to some particular solubilization solution.

The specification also provides no basis for the construction that Amgen proposes. Amgen cites to portions of the specification that purportedly teach "dilut[ing]" the solubilization solution when forming the refold solution. *See* '997 Patent at 19:25–27 ("[T]he protein solution was diluted in to a refold buffer . . . ."); *id.* at 20:48–50 (similar). Amgen misreads the specification with respect to these examples and embodiments. Diluting the solution *in to* the refold buffer does not suggest that components of the solubilization solution may be removed from the solution prior to forming the refold solution. Diluting one solution "in to" another, in that context, is synonymous with "mixing." That is, when one solution mixes with another, the concentrations of the components of each solution will be reduced, *i.e.*, diluted, in the resulting solution because of the increased volume and presence of other solutes. But this does not suggest that the solubilization solution or its components may otherwise be altered *prior to* forming the refold solution. Amgen has not identified any intrinsic evidence to support such a broadening construction.

Amgen also makes much ado about the fact that "the solubilization solution" will now contain the protein solubilized in Step (a). This, in their view, justifies their position that two solutions in Step (a) and Step (b) need not be the same. The Court does not agree. Claim 9 Step (b) states that the "refold solution" "*compris[es]* the solubilization solution and a refold buffer . .

." '997 Patent at 22:44–50 (emphasis added). Because the open-ended "comprising" is used to enumerate the components of the refold solution, additional components, such as the now-solubilized protein, can be present in the resulting solution. *See generally Smith & Nephew, Inc. v. Ethicon, Inc.*, 276 F.3d 1304, 1311 (Fed. Cir. 2001). In summary, the Court concludes that "the solubilization solution" refers to the solubilization solution formed in Claim 9, Step (a). There is insufficient support in the '997 Patent claims and specification to depart from this natural and plain reading of the claim language.

b. Refold Buffer

Mylan argues that Amgen attempts to "redefine" the term "buffer" with its proposed construction. (Mylan Opening Br. at 18). Amgen's own expert states that "the word "buffer" refers to a solution that resists changes in pH, but the same term is also commonly used in the art to refer to liquid preparations in biochemistry generally, regardless of whether such a preparation resists pH changes." (Willson Dec. ¶ 44, ECF No. 108). The claim language itself explicitly defines the "refold buffer" as a solution "comprising one or more of the following: (i) a denaturant; (ii) an aggregation suppressor; (iii) a protein stabilizer; and (iv) a redox component." '997 Patent at 22:45–50.

A patentee may act as its own lexicographer and redefine claim terms in the specification, but must "clearly express an intent to redefine the term." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012). But, "[t]he standards for finding lexicography are . . . exacting." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014). The Court concludes that such standards have not been met here. The '997 Patent specification speaks to the function of the "buffering component" of the refold solution, '997 Patent at 15:5–7, but does not, explicitly or otherwise, attempt to assign anything

other than the ordinary meaning to the word "buffer." However, this is not the end of the inquiry. Disputed claim terms must be given their meaning in the context of the entire patent as an integrated instrument, and "the specification is always highly relevant" to this determination. *Trustees of Columbia Univ.*, 811 F.3d at1363–66 (quoting *Phillips*, 415 F.3d at 1315). So, the question is what a person of ordinary skill in the art would understand the term "refold buffer" to mean in the context of the entire patent.

In Amgen's view, a skilled artisan reading the '997 Patent would understand that the "refold buffer" would be a pH-buffered solution. Its main intrinsic support comes from column 15, lines 5–7 of the '997 Patent specification, which state "[t]he function of the buffer component of the refold solution is to maintain the pH of the refold solution and can comprise any buffer that buffers in the appropriate pH range." But it does not follow that a functional description of the "buffering component" must limit the "refold buffer" as a whole because the claim at issue does not list a "buffering component" as a component of the "refold buffer." The components of the buffer are listed in the claim language itself, and only a "denaturant," "aggregation suppressor," "protein stabilizer," and a "redox component" are provided. '997 Patent at 22:44–50. Certainly a "refold buffer," based on this claim language using the open-ended "comprising" term, *can* include a "buffering component." *See Smith & Nephew*, 276 F.3d at 1311. But the "refold buffer" does not require a "buffering component" to be considered a "refold buffer." In fact, because the "refold buffer" is described as "comprising *one or more* of the following," *id.* at 22:45, a solution containing only a denaturant, only an aggregation suppressor, only a protein stabilizer, only a redox component, or some combination thereof, would nonetheless be a "refold buffer" as claimed in Claim 9. Furthermore, Amgen has not identified any portion of the specification that indicates that the refold buffer is *required* to

"maintain the pH of the refold solution," even if the stated function of the unclaimed "buffering component" is to do so. Nor is the Court persuaded that "buffer component" is merely synonymous with "refold buffer." "[W]hen different words are used in a patent, it is presumed that they carry different meanings." *Novartis Pharms. Corp. v. Actavis, Inc.*, No. 12-366, 2013 WL 6142747, at *5 (D. Del. Nov. 21, 2013). Thus, importing such a limitation would not be further justified.

It is true that the specification teaches that some compounds may be a "buffer component" and some other component of the refold buffer. Exemplary "buffer component" compounds include arginine-based buffers, tris-based buffers, and CHAPS.[8] Arginine and tris salts are each defined as "protein stabilizers," *id.* at 5:61–62, and CHAPS is a listed "aggregation suppressor." *Id.* at 5:52. And, by example, one "refold buffer comprises arginine, urea, glyercol, cysteine, and cystamine." *Id.* at 15:15–18. In this example, arginine could function both as the aggregation suppressor and buffering component. *See id.* at 4:45–51. But unless the specification indicates that the claims are to be limited to specifically disclosed embodiments, the Court will not so limit the claim scope. *See Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1327–28 (Fed. Cir. 2002) ("Absent such clear statements of scope, we are constrained to follow the language of the claims, rather than that of the written description.") (citing *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985)). Here, the specification indicates that the "arginine, urea, glyercol, cysteine, and cystamine" refold buffer is only "one embodiment" and "the composition of an [sic] refold buffer will vary with the protein being purified." '997 Patent at 15:14–18. The specification broadly discloses various compounds that

[8] The CAS Registry Number, which is a unique numerical identifier for chemical substances, for CHAPS is 75621-03-3. *See Common Chem.*, Am. Chem. Soc'y, http://www.commonchemistry.org/ChemicalDetail.aspx?ref=75621-03-3 (last visited Nov. 15, 2018). CHAPS is also known as 3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate. *Id.*

could be denaturants, aggregation suppressors, protein stabilizers, and redox components. *Id.* at 2:43–60. The claim states that a solution containing only one of these compounds could be a "refold buffer," and not all of the listed compounds have the ability to maintain pH.

In summary, Amgen's own expert explains that a "buffer" can refer generally to solutions used in biochemical applications regardless of their ability to maintain pH. The language of the claim itself lists four components that, in combination or individually, can comprise a "refold buffer." A "buffer component," which is the only component that is described in the specification based on its function/ability to maintain pH, is not among the claimed components. Thus, there is no basis to limit a "refold buffer" to "pH buffered" solutions.

c. Conditions to Refold into Biologically Active Form

Mylan also accuses Amgen of seeking to import an unjustified functional limitation into the claim by requiring that the resulting solution "provid[e] the conditions for the protein to refold into its biologically active form." Amgen argues that this construction "make[s] clear that the refold solution fulfills its purpose in the invention[.]" (Amgen Reply Br. at 12) (citing '997 Patent at 12:29–32). The Court does not agree. This limitation appears nowhere in the claim language and Amgen's cited passage from the specification discusses the importance of denaturing the inclusion bodies so that the protein "can be extracted and refolded into a biologically active form." '997 Patent at 12:29–32. Though this could be read as suggesting that the refold solution must provide appropriate conditions for the protein to be refolded into its biologically active form, this is too vague of an example and insufficient support to import such a limitation into the disputed term when no such limitation appears in the claim language.

In sum, the Court concludes that Amgen's proposed additional limitations are inappropriate and will not be imported into this disputed term. However, the Court does not

agree with Mylan in that no construction of this term is necessary because adopting the plain language of the term would not settle the "fundamental dispute regarding the scope" of this term. *O2 Micro*, 521 F.3d at 1362. In particular, solely adopting the plain language of the claim would not make clear that "the solubilization solution" in this term must refer to the particular "solubilization solution" recited earlier in the claim, and that "refold buffer" is defined explicitly in the claim and need not be a pH-buffered solution. Thus, the Court will construe the term in a manner that would reflect a skilled artisan's understanding of the term in light of the claims and specification of the '997 Patent, and in a manner that also settles the dispute between the parties regarding this term's scope. *See Exxon Chem. Patents, Inc. v. Lubrizol Corp.*, 64 F.3d 1553, 1555 (Fed. Cir. 1995) ("[T]he trial judge has an independent obligation to determine the meaning of the claims, notwithstanding the views asserted by the adversary parties.").

As explained in detail above, the Court concludes that "the solubilization solution" in this disputed term must be the same solubilization solution described and utilized in Step (a) of Claim 9. Amgen's proposed construction would allow for any solution that comprises one or more of the enumerated components of a "solubilization solution" to be considered "the solubilization solution," which is contrary to the use of the word "the" in the claim language and not supported by the specification. But, the Court does not believe that simply adopting the plain language "the solubilization solution," as Mylan suggests, would sufficiently settle the parties' dispute. The term "solubilization solution" does not have a plain meaning outside of the '997 Patent; it is defined explicitly in Step (a) of Claim 9. The Court agrees with Mylan insofar as "the solubilization solution" in the disputed term means just that—the "solubilization solution" as defined earlier in the claim. But the parties also disputed whether a "solubilization solution" that had some components removed (or added) would still be considered "the solubilization

solution" in the disputed term. As the Court explained, a subsequent reference to "the solubilization solution" must refer to a particular solubilization solution, so components of the utilized solubilization solution cannot be removed. The Court will adopt a construction that makes this resolution of the parties' dispute explicit: in the disputed term, "the solubilization solution" shall be construed as "the solubilization solution utilized in Step (a) of Claim 9."[9]

For similar reasons, the Court will construe "refold buffer" in the disputed term in a manner that explicitly resolves the parties' dispute. Amgen's proposed construction would add the limitation that a "refold buffer" must be a pH-buffered solution. As the Court explained, this additional limitation is not compelled by the specification nor supported by the claim language. However, adopting the plain language of the term would not resolve the parties' dispute because a "refold buffer" *could be* a pH-buffered solution. Thus, the Court's construction of the term makes explicit what a plain reading of the claims supports—a "refold buffer" is a solution that comprises one or more of the components listed in the language of the claim but need not necessarily contain a buffering component or have the ability to buffer pH.

For the foregoing reasons, the term "forming a refold solution comprising the solubilization solution and a refold buffer" shall be construed as "forming a solution comprising the solubilization solution utilized in Step (a) of Claim 9 and a solution comprising one or more of a denaturant, an aggregation suppressor, a protein stabilizer, and a redox component."

[9] The Court expresses no opinion at this time as to whether Step (a) and Step (b) of Claim 9 must be performed in a specific order. This issue was not briefed, or otherwise placed into controversy, by the parties. *See Vivid Techs.*, 200 F.3d at 803 ("[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy.").

2. "applying the refold solution to a separation matrix"

> **Amgen's Proposed Construction:** applying the refold solution to a separation matrix without intervening steps of dilution, centrifugation, dialysis, or precipitation[10]
>
> **Mylan's Proposed Construction:** applying the refold solution to a separation matrix without removing components or diluting the refold solution

This disputed term appears in Step (c) of Claim 9 of the '997 Patent. The *Sandoz* court construed a similar term in the '878 Patent. Simply put, Amgen and Mylan are rehashing the same contentions that Amgen and Sandoz quarreled over in the Northern District of California, 2016 WL 4137563 at *12–13, namely, whether the term allows for the removal of components of the refold solution after refolding but prior to applying the refold solution to the separation matrix.[11] The term construed by the *Sandoz* court included the word "directly" immediately before "applying" but was otherwise identical. This, according to Amgen, is not an immaterial difference between the two terms. Mylan's proposed construction is the verbatim construction adopted by the *Sandoz* court. *Id.* at *12.

As a preliminary matter, the text of Claim 9 of the '997 Patent is plainly broader than the corresponding claim of the '878 Patent that was construed by the *Sandoz* court because the '878 Patent claims "directly applying the refold solution to a separation matrix" rather than just "applying the refold solution to a separation matrix." *Compare* '878 Patent at 22:21–23 *with* '997 Patent at 22:51–53. And, the present dispute cannot be determined simply by consulting the plain meaning of the term "applying." Both applying a solution without removing components or

[10] Amgen initially proposed a construction that would have limited this term to column chromatography techniques. Amgen conceded in its Reply brief that it would strike that limiting language. (Amgen Reply Br. at 20, ECF No. 114). This language therefore reflects that concession.

[11] Here, as in *Sandoz*, both parties agree that "the patent teaches a method of purification that does not require dilution of the refold solution." *Sandoz*, 2016 WL 4137563 at *12.

performing intermediate processing steps as well as applying a solution after some processing steps would fall within the plain meaning of the term. Thus, the specification and other evidence must be examined. *Phillips*, 415 F.3d at 1314.

a. Prosecution History Disclaimer

Both Amgen and Mylan assert that the prosecution history of the '878 and '997 Patents supports their respective proposed constructions. Indeed, the prosecution history of the '878 Patent was a key consideration in the *Sandoz* court's decision. The *Sandoz* court concluded that "directly" in the context of "directly applying," must mean that there are no intermediate steps between protein refolding and purification in part because the patentee, during prosecution of the '878 Patent, distinguished a prior art reference by emphasizing that the prior art method required specific intermediate processing steps prior to applying the refold solution to a separation matrix. 2016 WL 4137563 at *13. To clarify this point, the patentee amended the '878 Patent's claim to include the word "directly." *Id.* Mylan argues that Amgen equated "applying" and "directly applying" during the prosecution of the '878 Patent, thereby disclaiming "applications" of the refold solution to the separation that are not "direct applications." In Mylan's view, this commands that the *Sandoz* court's construction of "direct applying" is binding on this Court's construction of "applying."

Prosecution history disclaimer applies "where the patentee has unequivocally disavowed a certain meaning to obtain his patent" and "narrows the ordinary meaning of the claim congruent with the scope of the surrender." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1324 (Fed. Cir. 2003). Disclaimers made during the prosecution of parent patent applications can apply to later-filed child applications, even if the child applications are filed with broader claims. *Hakim v. Cannon Avent Grp., PLC*, 479 F.3d 1313, 1317–18 (Fed. Cir. 2007); *see also Wang*

Labs., Inc. v. Am. Online, Inc., 197 F.3d 1377, 1383–84 (Fed. Cir. 1999) (applying prosecution history disclaimer to a continuation-in-part application because the arguments giving rise to the disclaimer concerned common subject matter of the parent application and the later-filed continuation-in-part application). Such a disclaimer can be rescinded, but this rescission must appear "sufficiently clear[ly]" in the prosecution history "to inform the examiner that the previous disclaimer, and the prior art that it was made to avoid, may need to be revisited." *Hakim*, 479 F.3d at 1318. But, "[i]n general, a prosecution disclaimer will only apply to a subsequent patent if that patent contains the same claim limitation as its predecessor." *Regents of Univ. of Minn. v. AGA Med. Corp.*, 717 F.3d 929, 943 (Fed. Cir. 2013) (collecting cases).

The '997 Patent issued from a divisional application of U.S. Patent Application No. 12/822,990, which eventually issued as the '878 Patent. The relevant prosecution history of these two patents is as follows. During prosecution of the '878 Patent, the examiner rejected Claims 9–15 and 17–20 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 7,138,370 (the "'370 Patent"). ('878 Patent File History Excerpt at 10–11, ECF No. 102-10). The patentee argued that the '370 Patent "teaches . . . that the refolded protein is subject to dialysis, precipitation, and centrifugation" and thus "differs markedly from the direct application of refold solution to the separation matrix." (*Id.*) (citing '370 Patent at 76:51–59). In other words, the patentee made clear that if the refolded protein is "subject to dialysis, precipitation, and centrifugation" then it has not been "directly applied." The examiner maintained the rejection because "[t]he claims [were] not limited to a method requiring direct application of refold solution to the separation." ('878 Patent Office Action at 7, ECF No. 102-11). In response, the patentee amended Claim 9 to add the word "directly" preceding "applying" to clarify that, for the

'878 Patent, the claims were *only* claiming direct applications of the refold solution. (*See* '878 Patentee Response at 7, ECF No. 102-12). This amended claim issued.

The patentee made similar, but broader, arguments in response to the examiner's § 102(b) rejection during the prosecution of the '997 Patent. Claims 9–15 and 17–20 of the '997 Patent were also initially rejected under 35 U.S.C. § 102(b) as being anticipated by the '370 Patent. ('997 Patent File History Excerpt at 8–9, ECF No. 101-2). The patentee argued that the '370 Patent did not anticipate the claims as written because it "does not recite forming a refold solution and applying the refold solution to a separation matrix" and, conversely, only "recites that the refolded protein is subject to dialysis, precipitation, and centrifugation" prior to loading the solution onto a column. (*Id.* at 22). The examiner's rejection was then "withdrawn in light of applicant's arguments thereto." (*Id.* at 28). The patentee explicitly argued while prosecuting the '997 Patent that "applying" (rather than "directly applying") the refold solution does not include the steps of "dialysis, precipitation, and centrifugation" and unequivocally disavowed this claim scope. *Omega Eng'g*, 334 F.3d at 1324. The issue is whether the term should be further limited.

The specifications of the '878 and '997 Patents are essentially identical. The claims at issue differ by only one word—"directly." But, this difference is a crucial one. Mylan essentially asks the Court to write in the word "directly" to the '997 Patent's claim whereas that term was explicitly part of the claim language when the *Sandoz* court construed the disputed terms in the '878 Patent. "[T]he doctrine of prosecution disclaimer generally does not apply when the claim term in the descendant patent uses different language." *Ventana Med. Sys., Inc. v. Biogenex Labs., Inc.*, 473 F.3d 1173, 1182 (Fed. Cir. 2006). The subject matter of the two patents may be the same, but the claim scope and language are not.

Hakim is a close factual analog to the instant case, but there a crucial difference in the prosecution history of the patents here. In *Hakim*, the patentee distinguished the prior art for a drinking device by clarifying that an "opening" in its claimed device was a "slit," and this feature distinguished the device over the prior art. 479 F.3d at 1316. The patentee then received a notice of allowance for the claims that claimed a "slit" rather than an "opening." *Id.* Sometime thereafter, the patentee filed a continuation application that substituted "opening" for "slit" in the claims, filed along with an attorney letter stating that the patentee intended to broaden the claims. *Id.* The claims issued without rejection. *Id.* The Federal Circuit held that the patentee had disclaimed "openings" that were not "slits" based on the arguments presented in the parent application, notwithstanding the patentee's intention to broaden the claims, because there was no "further prosecution" of the broader claims. *Id.* at 1317.

This situation is different insofar as there *was* further prosecution on the broader patent claims of the '997 Patent. The patentee, during prosecution of the '878 Patent, amended the rejected claim to add the term "directly" in order to clarify that the '878 Patent was *only* claiming direct applications of the refold solution. This amendment secured issuance of the patent. The '997 Patent did not have this limitation. Continuing patent applications may be utilized in order to pursue broader claims. *See Symbol Techs., Inc. v. Lemelson Med., Educ. & Res. Found.*, 422 F.3d 1378, 1385 (Fed. Cir. 2005). The examiner referenced the same prior art reference, the '370 Patent, but in the '997 Patent prosecution, the patentee was able to successfully argue for a broader scope for the term "applying" and no amendment was necessary. Unlike in *Hakim*, the examiner evaluated and considered arguments for a broader claim scope rather than issuing the claims without comment. The patentee disclaimed the intermediate steps of "dialysis, precipitation, and centrifugation" during the prosecution of the '997 Patent, but nothing more.

Disclaimer based upon statements made during patent prosecution is limited to the scope of the surrendered claim scope. *Omega Eng'g*, 334 F.3d at 1324.

b. Intrinsic Evidence

The specification speaks to the advantages of applying the refold solution directly to the separation matrix without engaging in intermediate processing steps. But, what is claimed is "applying" the refold solution, not "directly applying" the solution. "The patentee is free to choose a broad term and expect to obtain the full scope of its plain and ordinary meaning unless the patentee explicitly redefines the term or disavows its full scope." *Thorner*, 669 F.3d at 1367.

The '997 Patent teaches that direct application of the refold solution to the separation matrix, *i.e.*, without removing components of the refold solution, is advantageous over prior art methods that require the removal of components or other intervening steps between refolding and application to the separation matrix. '997 Patent at 4:60–5:6. This stated preference alone is an inadequate justification to apply a limiting construction. There is a "high bar to finding disavowal of claim scope through disparagement of the prior art in the specification." *Openwave Sys., Inc. v. Apple Inc.*, 808 F.3d 509, 517 (Fed. Cir. 2015). That bar has not been met here. The specification describes at least one embodiment wherein intermediate steps are performed on the refold solution prior to its application to the separation matrix. '997 Patent at 20:56–62 (describing how a sample of the refold solution was filtered to remove particulates prior to its application to the separation matrix); *id.* at 19:63–66 (similar). In contrast, "dilution" is much more consistently disparaged in the specification. It is described as "time-consuming and resource-intensive" and that "[t]he disclosed method eliminates the need for such a dilution step." *Id.* at 12:45–50. Conversely, the '997 Patent states that only that it as an "advantage" to directly apply the solution containing the refolded protein to the separation matrix "without the

need for diluting or removing the components of the solution required for refolding the protein." *Id.* at 15:50–55.[12] Even if it is an "advantage" to do so, it is not a required feature of the claimed invention. The cited portions of the specification that disclose intermediate filtration steps belie an assertion to the contrary.

On a final note, it has been discussed that the '878 and '997 Patents share a materially identical specification and many common claim terms. When this is so, claim terms should be interpreted "consistently across all asserted patents." *Sightsound Techs.*, 809 F.3d at 1316. Though *Sightsound* was in the context of two related patents asserted in a single appeal, the Court understands this as a statement of a general preference of claim construction. If "applied" were given the same construction as "directly applied" in the *Sandoz* case, it would necessarily render "directly" superfluous in the context of the '878 Patent. Such constructions are disfavored. *See Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005) ("A claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so."). Amgen's proposed construction gives effect to the disparate claim language between the '997 Patent and the '878 Patent. Mylan's does not.

For the foregoing reasons, "applying the refold solution to a separation matrix" shall be construed as "applying the refold solution to a separation matrix without intervening steps of dilution, centrifugation, dialysis, or precipitation."

[12] The Court also notes that Mylan's proposed construction—"without removing components of . . . the refold solution"—is broader than the above cited passage, which limits the removed components to those "required for refolding the protein." The "refold solution" may contain many other components besides those "required for refolding the protein." '997 Patent at 22:44–50.

3. "under conditions suitable for the protein to associate with the matrix"

> **Amgen's Proposed Construction:** under conditions suitable for protein to have specific reversible interactions with a separation matrix in order to effect the separation of protein from its environment
>
> **Mylan's Proposed Construction:** under conditions suitable for the protein to be purified to bind to the matrix
>
> (alternatively, plain and ordinary meaning)

This term also appears in Step (c) of the '997 Patent. Amgen conceded at oral argument that "associate" is synonymous with "bind." (Hearing Tr. at 114:6–22, ECF No. 160). The *Sandoz* court, after a thorough analysis of the '878 Patent's claim language and specification, reached the same conclusion. 2016 WL 4137563 at *16–17. This Court agrees. The specification of the '997 Patent equates "associat[ing]" with "binding" in several instances. *See, e.g.*, '997 Patent at 16:1–4 ("After the protein of interest has associated with the separation matrix the separation matrix is washed to remove unbound protein, lysate, impurities and unwanted components of the refold solution."); *id.* at 16:19–26 ("After the separation matrix with which the protein has associated has been washed . . . The protein of interest can be eluted using a solution that interferes with the binding of the adsorbent component of the separation matrix to the protein.") (emphasis added).

The remaining dispute is how to construe "the protein" in the disputed term. Amgen argues this protein can be any "protein expressed in a non-mammalian expression system." (Amgen Opening Br. at 16–17). Amgen argues that the patentee has chosen to broadly define "protein" to mean "any chain of at least five naturally or non-naturally occurring amino acids linked by peptide bonds," '997 Patent at 6:8–11, and thus "the protein" should not be limited to a specific protein.

The Court agrees with Amgen insofar as "protein" was explicitly defined by the patentee, and in the Court's estimation, was defined quite broadly. But, while this definition may "carr[y] forward to the meaning of "protein" in the claims," (Amgen Opening Br. at 17), this does not settle the issue in this disputed claim term. The parties are not disputing what "**a** protein" is in the context of the '997 Patent, but rather what "**the** protein" is in the context of this disputed claim term. Antecedent basis commands the conclusion that "the protein" must refer to "a protein expressed in a non-mammalian expression system," as that is the only instance in Claim 9 where the word "protein" is introduced with an indefinite article. *Wi-LAN*, 811 F.3d at 462 ("Subsequent use of the definite articles "the" or "said" in a claim refers back to the same term recited earlier in the claim."). But, more particularly, "the protein" must refer to "the protein to be purified."

The word "protein" is preceded by "the" in every mention of "protein" in Claim 9 following its introduction in the claim's preamble. This language is fatal to Amgen's proposed construction. Amgen's construction literally writes out "the" from the claim language. That is, under Amgen's construction, the claimed method is satisfied when the refold solution is applied to a separation matrix under conditions such that *any* "chain of at least five naturally or non-naturally occurring amino acids linked by peptide bonds" may associate with the matrix. The plain language of the claim is not so broad. Moreover, a disputed claim term must be construed in the context of the entire claim. *Phillips*, 415 F.3d at1314 ("[T]he context in which a term is used in the asserted claim can be highly instructive."). Amgen's construction makes little sense when read in the context of the entire claim. The stated purpose of the claimed method, in the claim preamble, is to "purify[] a protein expressed in a non-native limited solubility form in a non-mammalian expression system." '997 Patent at 22:36–38. Each of the steps of the claimed

method drives toward that goal, and the steps do so by explaining how "the protein" (which must be the protein introduced in the preamble) is manipulated. *Id.* at 22:39–55 (explaining how the protein is solubilized, loaded onto a separation matrix, washed, and eluted). As such, the preamble gives "life, meaning, and vitality" to the claims and "has the import that the claim as a whole suggests for it." *Bell Commc'ns Research, Inc. v. Vitalink Commc'ns Corp.*, 55 F.3d 615, 620–621 (1995) (quoting *Kropa v. Robie*, 187 F.2d 150, 152 (C.C.P.A. 1951)). The claim loses meaning without such a consideration, as all of the steps in Claim 9 describe how a protein is purified.

The Court notes that the claim language is not limited to purifying a particular protein. That is, in the Court's view, the claim is broad enough to cover a method that is capable of purifying more than one type of protein. But it is clear from reading this disputed term in the context of the claim and specification that "the protein" must refer to "the protein to be purified," whatever that protein may be. For the foregoing reasons, the Court concludes that "under conditions suitable for the protein to associate with the matrix" shall be construed as "under conditions suitable for the protein to be purified to bind to the matrix."

4. "washing the separation matrix"

> **Amgen's Proposed Construction:** applying a solution to the separation matrix, which application has the effect of removing unbound protein, lysate, impurities, and unwanted components of the refold solution from the separation matrix while preserving interactions between the protein and the separation matrix
>
> **Mylan's Proposed Construction:** applying a solution to remove unbound protein, lysate, impurities, and unwanted components of the refold solution from the separation matrix while preserving binding of the expressed protein
>
> (alternatively, plain and ordinary meaning)

This term appears in several claims of the '997 Patent, including Step (d) of Claim 9. The Court has already concluded that "associate" is synonymous with "bind" and that "the protein" refers to "the protein to be purified." The parties appear to agree on the remaining construction of this term. Thus, the term "washing the separation matrix" shall be construed as "applying a solution to remove unbound protein, lysate, impurities, and unwanted components of the refold solution from the separation matrix while preserving binding of the protein to be purified."

5. "eluting the protein from the separation matrix"

> **Amgen's Proposed Construction:** applying a solution to the separation matrix, which application has the effect of reversing the interactions between the protein and the separation matrix[13]
>
> **Mylan's Proposed Construction:** applying a solution that reverses the binding of the purified protein to the separation matrix
>
> (must occur after the "washing the separation matrix" step)
>
> (alternatively, plain and ordinary meaning)

This term also appears in several claims of the '997 Patent and follows the "washing" step described above as the final step of Claim 9. As discussed, "associate" is synonymous with "bind," the process is not limited to column chromatography, and "the protein" means "the protein to be purified." The remaining question is whether this term should be construed to necessarily occur after the washing step.[14] Amgen does not contend that the elution step can occur before the washing step, rather, their argument is that the steps can occur simultaneously (at different points) within a column. (Amgen Reply Br. at 25–26). The claim itself does not state that the listed steps must occur in a particular order. When this is so, "the steps are not ordinarily

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[13] Once again, Amgen initially proposed a construction that would have limited this term to column chromatography techniques. Amgen conceded this limitation in its Reply brief by striking this limiting language. (Amgen Reply Br. at 27). This language therefore reflects that concession.

[14] This is an issue on appeal in the *Sandoz* case. (Amgen Appeal Br. at 3).

construed to require one." *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1342 (Fed. Cir. 2001). But, "a claim requires an ordering of steps when the claim language, as a matter of logic or grammar, requires that the steps be performed in the order written, or the specification directly or implicitly requires an order of steps." *Mformation Techs., Inc. v. Research in Motion, Ltd.*, 764 F.3d 1392, 1398–99 (Fed. Cir. 2014) (quoting *TALtech Ltd. v. Esquel Apparel, Inc.*, 279 F. App'x 974, 978 (Fed. Cir. 2008)) (internal quotation marks omitted).

The Court agrees that the specification teaches that eluting cannot occur before washing *begins*. *E.g.*, '997 Patent at 16:19–24 ("After the separation matrix with which the protein has associated has been washed, the protein of interest is eluted using an appropriate solution . . ."). Relatedly, the specification teaches that the purpose of the washing step is "to remove unbound protein, lysate, impurities and unwanted components of the refold solution," *id.* at 16:2–4, and the pH range of the wash buffer is "chosen to . . . preserve protein binding." *Id.* at 16:13–14. The elution solution, on the other hand, "interferes with the binding of the adsorbent component of the separation matrix to the protein." *Id.* at 16:24–28. The elution thus cannot begin before the washing step, as the elution step is meant to interfere with a protein's bond to the separation matrix, which the washing step is meant to preserve. There would be no bond for the wash buffer to "preserve" if the elution step occurred prior to the washing step. (Georgiou Dec. ¶ 144, ECF No. 111-3).

However, the Court does not agree that the claim discloses "a natural, logical order of steps" that requires that the elution step occur after washing has been *completed*. It would make logical sense that the protein cannot be eluted prior to the washing step, as various contaminants would also be eluted with the protein of interest and would compromise the protein purification

process. But, given that elution can occur in a gradient fashion, *e.g.*, '997 Patent at 20:63–21:3, or that additional washing and elution steps may be necessary to fully purify a protein, *id.* at 16:36–38, there is nothing in the specification that would limit the order of steps such that *all* washing must be completed before *any* elution begins. In fact, the specification suggests that the opposite is true—some washing can occur after elution begins, and may be necessary to completely purify the protein. More importantly, the specification teaches that an exemplary embodiment of the invention can be carried out in a "column format." *E.g., id.*, at 16:56–67. Column chromatography separation techniques are well-known in the art, *id.* at 16:59–60, and according to Amgen's expert, those of ordinary skill in the art would understand that a column is not allowed to "run dry" at any time during the process. (Willson Dec. ¶ 108). In other words, at given points in the column, "washing" and "eluting" will occur simultaneously within the column. For example, the elution solution can be introduced to the top of the column as the washing buffer continues to flow downward through the separation matrix. Importantly, there is nothing in the claims nor the specification that would *require* that the washing and eluting steps could not occur simultaneously within a separation matrix, and thus adopting a construction that would necessitate that the steps be performed in a certain order as completely distinct steps would be unjustified.

For these reasons, the Court concludes that Mylan's proposed construction is too restrictive to adopt. However, the specification and logic dictate that the elution step cannot begin prior to the washing step beginning. Accordingly, the Court concludes that "eluting the protein from the separation matrix" shall be construed as "applying a solution that reverses the binding of the purified protein to the separation matrix" and that this step cannot begin before the washing step begins.

The '707 Patent

The '707 Patent is entitled "Process for Purifying Proteins" and issued on September 25, 2012. Amgen is the current assignee. The patent generally discloses a protein purification process utilizing hydrophobic interaction chromatography (HIC).'707 Patent at 1:13–15. HIC techniques purify proteins on the basis of hydrophobic interactions between hydrophobic regions of the targeted proteins and hydrophobic regions of a separation matrix. *Id.* at 1:36–39. Purification processes utilizing HIC techniques are well-known in the art. *See generally id.* at 1:46–51. The '707 Patent describes a process wherein the targeted proteins are dissolved in a mobile (or solution) phase that contains a salt buffer, and various contaminants, other proteins, and cellular debris that are to be removed from the solution. *Id.* at 3:53–61. The mobile phase flows past a stationary phase, which contains a separation matrix, within the column. *Id.* As the mobile phase flows past the stationary phase, regions of the targeted proteins in the mobile phase interact with regions of the stationary phase and separate out of the solution. *Id.* The salt within the mobile phase is utilized to expose the hydrophobic regions of the proteins to encourage the interactions between the proteins and the stationary phase. *Id.* at 1:41–46. "Dynamic capacity" refers to 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 a column before elution." *Id.* at 3:65–4:3. The '707 Patent teaches a process wherein a protein, first salt, and a second salt in solution are loaded onto a HIC column such that the dynamic capacity of the column is increased. *Id.* at 1:66–2:3, 2:39–43. By increasing the dynamic capacity, this process can decrease the number of cycles needed to purify a protein, thereby saving time and resources. *Id.* at 2:42–46. All of the disputed terms appear in Claim 1 of the '707 Patent.

1. "such that the dynamic capacity of the column is increased for the protein"

> **Amgen's Proposed Construction:** such that the dynamic capacity of the hydrophobic interaction chromatography column for the protein that is achieved by using a combination of a first salt and a second salt, each at a reduced concentration compared to the concentration of either salt when used alone, is greater than the dynamic capacity of the column for the protein that is achieved by using a single salt at a higher concentration
>
> **Mylan's Proposed Construction:** plain and ordinary meaning, no construction necessary

Mylan asserts that this term does not require construction beyond construing it as having its plain and ordinary meaning. The construction of this term is necessary to validity and infringement analysis. *O2 Micro*, 521 F.3d at 1361–62. We know this because Mylan has already alleged that this claim is invalid because it fails the written description requirement of 35 U.S.C. § 112. (Invalidity Contentions, ECF No. 106-2). This term was specifically cited. (*Id.*). Thus, the Court is required to address its construction.

The Court concludes that a skilled artisan reading the '707 Patent in its entirety would understand that an increase in the dynamic capacity of the column through using a salt pair would be in reference to the dynamic capacity of the column when using a single salt. The abstract of the '707 Patent explicitly makes this comparison when describing what the "increase" in dynamic capacity refers to. The specification also teaches that one of the primary advantages of this invention is that a two salt buffer system will "result[] in decreased number of cycles required for purifying a batch of protein" because of "an increase in dynamic capacity . . . compared with the dynamic capacity achieved by single salts." '707 Patent at 2:39–42. Thus, a skilled artisan would understand that utilizing a two salt buffer system can result in a more efficient process *when compared to* single salt systems. Provided examples of specific embodiments also consistently reference increases in dynamic capacities using salt pairs in

reference to the dynamic capacity achieved using a single salt. *See id.* at 13:59–64, 14:42–45, 14:61–63.

Further, the '707 Patent states in several passages that one of the chief features of *the* invention is the ability to choose salt pairs in reference to concentrations of single salts, to decrease the concentration of at least one of the salts, and to thereby increase the dynamic capacity of the column.'707 Patent abstract; *id.* at 2:39–43; *id.* at 5:25–33; *see also id.* at 12:37–40. The fact that this feature is described in reference to "the present invention," rather than just a particular embodiment thereof, is particularly significant. Limitations from the specification are generally not to be read into the claims. *See generally Comark*, 156 F.3d at 1186–87. But, "when a patent [] describes the features of the 'present invention' as a whole, this description limits the scope of the invention." *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1308 (Fed. Cir. 2007). Descriptions using language such as "the present invention includes," "the present invention is," and "all embodiments of the present invention are" have been found to be limiting. *Luminara Worldwide, LLC v. Liown Elecs. Co.*, 814 F.3d 1343, 1353 (Fed. Cir. 2016) (collecting cases). The '707 Patent uses language in the same vein:

> The two salt buffers **of the present invention** result in an increase in dynamic capacity of an HIC column for a particular protein compared with the dynamic capacity achieved by single salts.

'707 Patent at 2:39–43. Thus, it is plain that "increase in dynamic capacity" in the context of this invention and the '707 Patent is in reference to the dynamic capacity of the column when a single salt is utilized.

A closer question is Amgen's additional proposed limitation that the comparator is the dynamic capacity achieved "by using a single salt at a higher concentration" than the concentration of either of the salts in the salt pair. While the specification is clear that the

dynamic capacity of a column using a single salt buffer is a proper comparator for the "increase" in dynamic capacity when using a two-buffer system, it does not follow that each salt must be used in a reduced concentration compared to the concentration of either salt when used alone. The cited portions above from the specification are not so limiting. Further, Table 1 in the '707 Patent cuts against this assertion. *See* '707 Patent at 13:40–58. The table lists the dynamic capacity of a HIC column using salt pairs and the dynamic capacity of 0.55 M Citrate, 0.5 M Phosphate, 0.8 M Sulfate, and 1.2 M Acetate in single salt systems. Most of the listed results for salt pairs include each salt at a lower concentration than their concentrations when used in a single salt system. But, two of the entries (0.35 M Phosphate/0.6 M Citrate and 0.3 M Citrate/0.6 M Phosphate) utilized a salt species in a salt pair that was present in a higher concentration than when used as a single salt. *See also id.* at 2:13–15 ("These combinations of salts allow for a decreased concentration of *at least one of the salts* to achieve a greater dynamic capacity[.]") (emphasis added). Even if the '707 Patent suggests that the dynamic capacity of a column *can* be increased through using salts in a pair at a lower concentration than the concentration of either of the salt species alone, it does not state that this is *necessary* to increase the dynamic capacity of the column, or that this is a required comparator. The portion below, cited by Amgen, is not to the contrary:

> According to the present invention a first salt and a second salt are selected which have differing lyotropic values. This combination of salts acts together to increase the dynamic capacity of the HIC column for a particular protein. It has been found according to the present invention that each salt in combination **can** be provided at a lower concentration that [sic] the concentration of the salt alone to achieve a higher dynamic capacity using a single salt.

'707 Patent at 5:25–33 (emphasis added). This use of the word "can," despite being described in reference to "the present invention," clearly indicates that the ability to provide each

salt at a lower concentration when paired is optional. Accordingly, the Court will not import such a limitation. *See Intel Corp.*, 946 F.2d at 836 ("[W]here a specification does not *require* a limitation, that limitation should not be read from the specification into the claims.") (emphasis in original).

The Court will not construe this term to have its plain and ordinary meaning, as Mylan proposes, because the word "increase," though it has a plain meaning, must be read in the context of the claims and specification of the '997 Patent. To determine if there has been an "increase" in dynamic capacity, there must be some initial dynamic capacity to which the new dynamic capacity can be compared. This comparator is not within the plain language of the claim, but it is apparent when the term is read in the context of the entire patent. As explained, the Court concludes that a skilled artisan would understand that an "increase" in the dynamic capacity for the protein when using a claimed salt pair would be in reference to the dynamic capacity of the protein when a single salt is utilized. However, the Court does not believe that the intrinsic evidence supports the conclusion that a skilled artisan would necessarily understand that each salt in the salt pair would be provided at a lower concentration than a single salt, as Amgen proposes. Thus, an intermediate construction is warranted. *See Exxon Chem. Patents*, 64 F.3d at 1555. For the foregoing reasons, the Court construes "such that the dynamic capacity of the column is increased for the protein" as "such that the dynamic capacity of the hydrophobic interaction chromatography column for the protein that is achieved by using a combination of a first salt and a second salt is greater than the dynamic capacity of the column for the protein that is achieved by using a single salt."[15]

[15] The Court expresses no opinion on whether this claim satisfies the definiteness standard established by *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120 (2014), at this time. A lack of definiteness is an invalidity defense, *id.*, and an invalidity defense must be proven by clear and convincing evidence. *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 95 (2011). Because of the disparate evidentiary burdens between claim construction and proving

2. "mixing a preparation containing the protein with a combination of a first salt and a second salt"

> **Amgen's Proposed Construction:** forming the mobile, or solution, phase, which contains the protein, a first salt, and a second salt
>
> **Mylan's Proposed Construction:** plain and ordinary meaning, no construction necessary

The term must be construed because the parties have put it into dispute. *O2 Micro*, 521 F.3d at 1360–63. Amgen proposes a construction that would equate "mobile, or solution, phase" with "a preparation containing the protein with a combination of first salt and a second salt." The Court agrees with Mylan in that such a construction would be inappropriate. In this technological context, the words "mobile" and "solution" phase appear to the Court to have well-established and understood plain meanings. Mylan and Amgen's respective experts both referred to the "mobile phase" of a HIC column as any solution that flows through the column and interacts with the stationary phase. (Jungbauer Dec. ¶ 80, ECF No. 111-1; Willson Dec. ¶ 42). The "mobile phase" need not contain any particular component or solution. (Jungbauer Dec. ¶ 81).

"[T]he specification and prosecution history only compel departure from the plain meaning in two instances: lexicography and disavowal." *GE Lighting Solutions, LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir. 2014) (citing *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012)). And while a patentee may act as her own lexicographer, the patentee must "clearly set forth a definition" and "clearly express an intent to define the term." *Thorner*, 669 F.3d at 1365. The patentee has not met this "exacting" standard here. *See GE Lighting*, 750 F.3d at 1309.

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invalidity, as well as the somewhat minimal briefing on the definiteness of this claim, the Court declines to determine whether this claim is definite at this time. The Court does not fault the parties for choosing to focus their efforts on more pressing claim construction issues in their briefing. The purpose of claim construction is to give meaning to the claims. The invalidity battles will be fought another day.

In the Court's view, the '707 Patent specification confirms that the patentee intended for the term "mobile phase" to retain its plain and ordinary meaning as explained by Drs. Jungbauer and Willson. The solution that Amgen equates to the "mobile phase"—a preparation containing the protein, a first salt, and a second salt—is defined as "the protein/buffered salt solution mixture." '707 Patent at 6:64–66. Had the patentee intended to redefine "mobile phase" to be limited to solutions of this particular composition, the patentee would have done so at that instance. To the extent that the '707 Patent supports *any* departure from the plain and ordinary meaning of the term, such a departure would not support Amgen's construction. According to the '707 Patent, "[t]he mobile phase of HIC according to the present invention is the two salt solution." '707 Patent at 6:41–42. Descriptions of "the present invention" such as this have been found to be limiting. *Luminara*, 814 F.3d at 1353.

Amgen has not identified any portion of the specification (nor has the Court) that mandates, or even suggests, that the "mobile phase" *must* contain the protein. In fact, both Mylan and Amgen's experts appear to agree that there will be applications wherein the mobile phase applied to the column *could not* contain the protein. For instance, both experts agree that the protein may be eluted from the column by decreasing the salt concentration in the mobile phase. (Willson Dec. ¶¶ 51, 56; Jungbauer Dec. ¶ 83). The '707 Patent specification confirms this understanding. '707 Patent at 7:1–3 (explaining that elution "can preferably be accomplished by decreasing the salt concentration of the buffer"). As explained by Dr. Jungbauer, "[d]uring elution, the solution applied to the column would not contain protein, as the purpose of elution is to reverse the binding of the protein to the column." (Jungbauer Dec. ¶ 89).

The parties have also placed into dispute whether this term and the term that follows ("loading the mixture onto a hydrophobic interaction chromatography column") must occur

sequentially in the order that they are listed in the claims. To reiterate, method claims do not ordinarily require that the steps must be performed in a particular order unless such an order is recited in the claims. *Interactive Gift Express*, 256 F.3d at 1342. But, if "as a matter of logic or grammar" the claim "requires that the steps be performed in the order written" or the specification provides such an implication, then the claim may be limited to a particular order. *Mformation*, 764 F.3d at 1398. Unlike the "washing" and "eluting" steps described above in the '997 Patent, the Court concludes that the "mixing a preparation" and "loading the mixture" steps must be performed in the order written.

First, the plain language of the claim supports such a conclusion. The significance of using "the" in reference to claim terms was discussed above. Here, the first step of the method is "mixing a preparation containing the protein . . ." and the second is "loading the mixture onto a hydrophobic interaction chromatography column." '707 Patent at 15:8–13 (emphasis added). The "mixture" is not otherwise defined in the claims, but it is clear from a reading of the patent claim that "the mixture" refers to the "mixture" formed when "a preparation containing the protein" is mixed with "a combination of a first salt and a second salt." *See id.* Because "the" is used to introduce "the mixture" in its subsequent mention in the second step, it must refer to the mixture formed in the previous step. *Wi-LAN*, 811 F.3d at 462.

This reference makes the situation analogous to *Mformation Technologies*. There, the Federal Circuit determined that a method claim claiming a method of remotely managing a wireless device required that the claimed steps be performed in a specific order. 764 F.3d at 1399–1400. This was, in part, because one of the steps was "establishing a mailbox for the wireless device at the server" and subsequent steps were "delivering the command from the mailbox at the server" and "transmitting the contents of the mailbox." *Id.* at 1394. The Federal

Circuit held that these steps "inherently require an order-of-steps" because "[a]s a matter of logic, a mailbox must be established before the contents of said mailbox can be transmitted." *Id.* at 1399–1400. *Function Media, L.L.C. v. Google, Inc.*, 708 F.3d 1310 (Fed. Cir. 2013), lends similar support. There, the Federal Circuit construed a patent directed to the creation and publication of customized electronic advertisements. *Id.* at 1314–15. One of the disputed terms was "a computer controller of the computer system processing and publishing the electronic advertisement." *Id.* at 1319. In particular, the parties disputed whether "processing" was in reference to the processing of ads that were already created or if it could also refer to the processing of raw information to generate new ads. *Id.* at 1319–20. Analyzing the claim language, the Federal Circuit determined that "the creation of the ad must happen before the processing begins" in part because "[t]he claim clearly states that the "processing" is done to the "electronic advertisement."" *Id.* at 1320.

This claim has a similar structure. It clearly states that "the mixture" is what is "load[ed] onto a hydrophobic interaction chromatography column." '707 Patent at 15:10–13. This strongly implies that "the mixture" must be formed before it is "load[ed]." As a matter of logic, something cannot be a "mixture" until its individual components are mixed. And therefore, "the mixture" cannot be "load[ed] . . . onto a hydrophobic interaction chromatography column" until after its components are mixed and the mixture is formed. Had the patentee intended that the mixture be formed within the column or on the separation matrix, the patentee could have listed the individual components of the mixture (the preparation of the protein and a combination of a first and second salt) as what is being "loaded." By using "the mixture," the patentee referred to the mixture formed in the preceding step through the use of a definite article.

The '707 Patent specification confirms this conclusion. Several passages indicate that "the mixture" of the protein and two salt solution is prepared *and then* the mixture is loaded onto the column. *See, e.g.*, '707 Patent at 6:60–66 ("The protein preparation is prepared by "conditioning" or mixing with the two salt buffered solution . . . *Next*, the protein/buffered salt solution mixture is loaded onto the column[.]") (emphasis added); *id.* at 12:52–63 ("This mixture was the hydrophobic interaction chromatography (HIC) load . . . *Then* the load mixture was loaded.") (emphasis added). This is unlike the "washing" and "eluting" steps above because those terms were two separate and distinct steps that were being performed on the column. As explained by the Court, there is no limitation that these steps could not occur at different points within a column at the same time. But here, the product of one step (the mixture) is utilized as soon as the next step begins (loading the mixture). Necessarily, the mixture cannot be loaded before it is formed.

For the foregoing reasons, the Court construes "mixing a preparation containing the protein with a combination of a first salt and a second salt" as having its plain and ordinary meaning and that this step must be completed prior to the "loading the mixture" step beginning.

3. "loading the mixture onto a hydrophobic interaction chromatography column"

> **Amgen's Proposed Construction:** causing the protein in the mobile phase to contact the hydrophobic groups on the matrix
>
> **Mylan's Proposed Construction:** plain and ordinary meaning, no construction necessary

The Court has already concluded that "the mixture" refers to the preparation prepared in the preceding step. The single remaining dispute between the parties in this term is what it means to "load" the mixture onto a column. Mylan views it simply: "loading" the mixture onto the column is just "the physical act of introducing the protein salt mixture onto the column." (Mylan

Resp. Br. at 48). Amgen, on the other hand, asserts that "loading" is "more precisely and accurately, causing the protein to contact the [hydrophobic interaction chromatography] matrix in the column." (Amgen Br. at 27).

The plain language of the claim does not resolve this dispute. "Loading" has multiple plain meanings, none of which simply equate the term to "introducing."[16] And, had the patentee intended to claim the simple action of "the physical act of introducing the protein salt mixture onto the column," the patentee could have employed any number of words that plainly described this process. For instance, the claim could have read "pouring the mixture," "introducing the mixture," "adding the mixture," and the like. The meaning of "loading" in this claim is "not immediately apparent" and thus the Court will examine the intrinsic evidence to understand how a skilled artisan would interpret this term. *Phillips*, 415 F.3d at 1314.

Amgen provided sufficient evidence from the specification to demonstrate that "load" in the context of this patent meant more than just introducing the mixture into the column. More particularly, the specification indicates that "load" specifically refers to interactions of the protein with the separation matrix. The claim itself is the starting point for claim construction. *Scanner Techs.*, 365 F.3d at 1303. The word "onto" (rather than "into") suggests that the mixture must contact the matrix within the column rather than simply being introduced into the top of the column. The specification supports this construction as well. For example, "dynamic capacity" is defined as "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 a column before elution. '707 Patent at 3:65-4:3. Thus, the specification teaches that protein that has been "loaded" is protein that has contacted the matrix of a column and remains on the column as the solution phase flows out.

[16] *See* Merriam-Webster, https://www.merriam-webster.com/dictionary/load (last visited Nov. 2, 2018).

But as the Court stated above, "the mixture" refers to the protein/salt mixture, and not more generally "the mobile phase." The protein is introduced into the column when "the mixture" is introduced into it, and thus cannot be "loaded" until at least after "the mixture" is formed and introduced into the column. For these reasons, the Court construes the phrase "loading the mixture onto a hydrophobic interaction chromatography column" as "causing the protein in the mixture to contact the hydrophobic groups on the matrix."

4. "between about 0.1 M and about 1.0"

> **Amgen's Proposed Construction:** approximately 0.1 M to approximately 1.0 M, depending on the characteristics of the particular salt
>
> **Mylan's Proposed Construction:** plain and ordinary meaning, no construction necessary. Alternatively, it should be understood to not encompass concentrations below 0.04 M.

The parties agree that this claim covers salt concentrations within the 0.1 M to 1.0 M range,[17] and because the word "about" is used, would also cover concentrations that fell slightly outside of the range on either the low or high end. *See Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1369–70 (Fed. Cir. 2005) (explaining that the ordinary meaning of "about" is "approximately" and that "about" should be given this meaning unless the patentee clearly redefines the term in the specification); *Quantum Corp. v. Rodime PLC*, 65 F.3d 1577, 1581 (Fed. Cir. 1995). Both parties advance additional limitations that are not within the plain language of the claim. Amgen contends that the construed term must include the limitation "depending on the characteristics of the particular salt" and Mylan asserts that the construed term should be understood to not encompass concentrations below 0.04 M.

[17] The Court concludes from reading the disputed term in the context of the entire claim that the second numerical value ("1.0") in the disputed term is referring to a concentration of the salt and thus will be construed and analyzed as "1.0 M" instead of "1.0."

a. Depending on the Characteristics of the Particular Salt

Amgen points to portions of the specification that state that "[t]he concentration of the salts used *according to the present invention* will depend on the characteristics of the particular salts."'707 Patent at 6:8–10 (emphasis added). This language is potentially significant. *Luminara*, 814 F.3d at 1353 ("When a patentee describes the features of the present invention as a whole, he implicitly alerts the reader that this description limits the scope of the invention.") (internal quotations omitted). But even so, importing Amgen's limitation would add confusion rather than clarity to the claim construction. The plain language of the claim already allows for a variation in salt concentration, namely, between about 0.1 M and about 1.0 M. Adding Amgen's limitation could suggest that the *range* of permissible salt concentrations itself could vary depending on the concentration of the particular salt, rather than the salt concentration chosen *within* the claimed range. There is no support in the '707 Patent's claim language or specification to warrant such a reading of the claim, and the Court declines the invitation to import one now. The claim language is sufficiently clear without Amgen's qualifier.

a. Prosecution History Disclaimer

Mylan conceded during the claim construction hearing that it would accede to a claim construction of about 0.1 M to about 1.0 M without reading in additional qualifiers.[18] But, Mylan also raised an argument in their briefing and later during the hearing that, based on prosecution history disclaimer, the claimed range should be understood to not encompass salt concentrations below 0.04 M. (Hearing Tr. at 260:16–22). The Court concludes for the reasons that follow that the term will not be further limited based on prosecution history disclaimer and, consistent with

[18] *See* Hearing Tr. at 254:13–16 ("All we are asking, Your Honor, is not to read in additional qualifiers and just leave it as about .1 to 1 without reading in depending on the . . ."); *id.* at 255:3–6 ("If we all agree, and it seems like we do, that there is a range of about .1 to about 1, then that settles it in our view. There is no reason to go any further than that.").

Mylan's concession, expresses no further opinion about the bounds of the claimed range at this time.

The meaning of "about" "depends on the technological facts of the particular case" and thus the use of "about" "avoids a strict numerical boundary to the parameter." *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217 (Fed. Cir. 1995). However, as the *Pall Corporation* case itself illustrates, a court, in construing disputed claim terms, may determine whether a particular value would or would not fall within the specified range. *Id.* at 1217–18 (examining the technological context of the claims at issue and determining that methylene to amide ratios of 4:1 did not fall within the claimed range of "about 5:1 to about 7:1").

The specification itself does not provide support to further limit the claimed range. Mylan's additional proposed limitation—that "about 0.1 M" should be understood to not encompass concentrations below 0.04 M—is premised on prosecution history disclaimer. The standards for prosecution history disclaimer were laid out in detail above and will not be repeated here. It bears repeating, however, that a patentee must "unequivocally" disavow a "certain meaning to obtain his patent." *Omega Eng'g*, 334 F.3d at 1324. "[V]ague or ambiguous" statements made during prosecution are insufficient for prosecution history disclaimer to attach. *Id.* at 1325.

In a parent application to the '707 Patent, the patentee distinguished a prior art method that utilized a 0.04 M sodium acetate and 0.04 M sodium phosphate salt pair by stating that this invention "does not teach or suggest combining the protein to be purified with the *particular combination of two salts, citrate and phosphate salts*, at concentrations of between about 0.1 M and 1.0 M." ('395 Patent File History Excerpt at 8–9, ECF No. 102-5) (emphasis in original). In this sense, the patentee made an unmistakable representation that, at least for acetate and

phosphate salt pairs, 0.04 M was *not* "about 0.1 M." Amgen argues that their position is still sound because this would only affect acetate and phosphate salt pairs, and not the other salt pairs that the '707 Patent claims.

Rather than "unequivocally" disclaiming salt concentrations less than 0.04 M for the claimed salt pairs of the '707 Patent's parent, it appears to the Court that the patentee only unequivocally disclaimed salt concentrations below 0.04 M for citrate and phosphate salt pairs. At minimum, it is ambiguous whether the patentee intended that salt concentrations, in a general sense, less than 0.04 M are less than "about 0.1 M." And further, the patent claimed only a citrate and phosphate salt pair. ('395 Patent File History Excerpt at 5). To secure the issuance of that claim, the patentee would have only needed to surrender concentrations pertaining to those salt pairs. The Court will not extend the scope of the disavowal beyond what was surrendered in order to secure the patent. *Omega Eng'g*, 334 F.3d at 1324 ("[T]he doctrine of prosecution disclaimer . . . narrows the ordinary meaning of the claim congruent with the scope of the surrender.").

Mylan also references the prosecution history of a related European patent, EP No. 1 711 512 B1, in support of its prosecution history disclaimer argument.[19] The Federal Circuit cautions against indiscriminate reliance on statements made to foreign patent offices, in part because patent laws and examination procedures differ from country to country. *See AIA Eng'g Ltd. v. Magotteaux Int'l S/A*, 657 F.3d 1264, 1279 (Fed. Cir. 2011). Statements made to foreign patent offices during the prosecution of foreign patent applications are "irrelevant to claim construction" if the statements "were made in response to patentability requirements unique to [foreign] law." *Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, 457 F.3d 1284, 1290 (Fed. Cir. 2006). The

[19] Amgen is also the inventor of this patent. The European Patent claims priority to PCT Application No. PCT/US04/23434. This PCT application and the '707 Patent claim priority to the same provisional application, U.S. Application No. 60/540,587.

context in which the allegedly disavowing statements was made is unclear from the submitted excerpt of the European patent's prosecution history. (ECF No. 111-19).

The Court notes that these statements to the European Patent Office might be considered relevant extrinsic evidence, *see Starhome GmbH v. AT&T Mobility LLC*, 743 F.3d 849, 858 (Fed. Cir. 2014), but in the Court's estimation, that question has not been developed in this proceeding. Thus, the Court expresses no opinion as to the weight or significance of the statements made to the European Patent Office. More importantly, Mylan conceded at the *Markman* hearing here that "[t]here is no reason to go any further," (Hearing Tr. at 255:3–6), than to conclude that this disputed term does not include the limitation "depending on the characteristics of the particular salt." The Court agrees. The legal determination of how low "about 0.1 M" can go need not be further addressed given Mylan's concession, and if it need be addressed at all, it would be more appropriately addressed after development of the issue in the specific context of this case. Thus, the term "about 0.1 M to about 1.0" shall be construed as "approximately 0.1 M to approximately 1.0 M."

IV. CONCLUSION

The Court construes the following disputed terms in the '997 Patent as follows:

"forming a refold solution comprising the solubilization solution and a refold buffer"	forming a solution comprising the solubilization solution utilized in Step (a) of Claim 9 and a solution comprising one or more of a denaturant, an aggregation suppressor, a protein stabilizer, and a redox component
"applying the refold solution to a separation matrix"	applying the refold solution to a separation matrix without intervening steps of dilution, centrifugation, dialysis, or precipitation
"under conditions suitable for the protein to associate with the matrix"	under conditions suitable for the protein to be purified to bind to the matrix

"washing the separation matrix"	applying a solution to remove unbound protein, lysate, impurities, and unwanted components of the refold solution from the separation matrix while preserving binding of the expressed protein
"eluting the protein from the separation matrix"	applying a solution that reverses the binding of the purified protein to the separation matrix. This step cannot begin before the washing step begins.

The Court construes the following disputed terms in the '707 Patent as follows:

"such that the dynamic capacity of the column is increased for the protein"	such that the dynamic capacity of the hydrophobic interaction chromatography column for the protein that is achieved by using a combination of a first salt and a second salt is greater than the dynamic capacity of the column for the protein that is achieved by using a single salt
"mixing a preparation containing the protein with a combination of a first salt and a second salt"	mixing a preparation containing the protein with a combination of a first salt and a second salt (plain and ordinary meaning) This step must be completed before the "loading the mixture" step begins.
"loading the mixture onto a hydrophobic interaction chromatography column"	causing the protein in the mixture to contact the hydrophobic groups on the matrix
"between about 0.1 M and about 1.0"	between approximately 0.1 M and approximately 1.0 M

An appropriate Order will issue.

Mark R. Hornak
United States District Judge

Dated: November 20, 2018

cc: All counsel of record