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

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