UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

AMGEN INC., et al., Plaintiffs, v. SANDOZ INC., et al., Defendants.	Case No. 14-cv-04741-RS Case No. 16-cv-02581-RS **ORDER GRANTING SUMMARY JUDGMENT OF NONINFRINGEMENT AND DENYING RULE 56(D) MOTION**

I. INTRODUCTION

Defendants Sandoz Inc., Sandoz International GmbH, Sandoz GmbH, and Lek Pharmaceuticals d.d. (collectively, "Sandoz") move for summary judgment as to both noninfringement and damages. Plaintiffs Amgen Inc. and Amgen Manufacturing, Limited (collectively, "Amgen") oppose summary judgment and move, in the alternative, pursuant to Rule 56(d), to defer a ruling on noninfringement until additional information is produced regarding a pending modification to Sandoz's allegedly infringing process. For the reasons explained below, Sandoz's motion for summary judgment of noninfringement is granted. The motion for summary judgment regarding damages is denied as moot. Amgen's Rule 56(d) motion is denied.[1]

[1] Sandoz and Amgen have filed multiple sealing motions regarding materials submitted as part of their summary judgment filings. Those motions (14-cv-04741, Dkt. No.'s 278, 289, 295, 298, 312, 324, 328, 332, 337; 16-cv-02581, Dkt. No.'s 116, 133, 134, 137, 151, 162, 166, 169, 174) are granted. Amgen additionally moved for leave to file an opposition to a request to strike made by Sandoz in one of its replies. The materials Sandoz seeks to strike are not relied on in this order. Accordingly, Sandoz's request to strike and Amgen's motion (14-cv-04741, Dkt. No. 333, 16-cv-02581, Dkt. No. 170) are denied.

II. BACKGROUND

Amgen and Sandoz compete to develop, manufacture, promote, and sell biopharmaceutical products. The products at issue here are filgrastim and pegfilgrastim. Filgrastim is the pharmaceutical analog of a protein that naturally occurs in the human body. It stimulates the production of a type of white blood cells ("neutrophils") vital to the human immune system and, accordingly, is useful for treating patients undergoing certain forms of cancer therapy (e.g., chemotherapy) that can cause neutrophil deficiency ("neutropenia"). Pegfilgrastim is a modified version of filgrastim that remains in the circulatory system for a substantially longer period of time and thus is "long acting." Amgen began selling filgrastim in 1991 under the brand name Neupogen® and launched a pegfilgrastim product, Neulasta®, in 2002. Sandoz brought to market an FDA-approved biosimilar filgrastim product, Zarxio®, in 2015. Sandoz also has submitted an application to offer a biosimilar pegfilgrastim product that is pending before the FDA.

As explained in the claim construction order, recombinant proteins like filgrastim are manufactured in a multi-step process. The process begins when scientists introduce human DNA into a host cell of a different species, such as *E. Coli* bacteria, causing the bacteria to produce human proteins. Before these proteins can be therapeutically useful, however, they must attain a three-dimensional shape. Trouble arises when the host cells produce proteins that lack this proper shape. These "unfolded" proteins accumulate in the host cell and form insoluble aggregates called "inclusion bodies." To remedy the problem, scientists break open (lyse) the host cell to release the inclusion bodies. They solubilize the inclusion bodies, mixing the proteins with various chemicals to create a solution. They then combine that solution with a "refold buffer" to cause the protein to take a workable, three-dimensional shape.

Once the protein has refolded, it must be separated from the chemicals used for solubilization and refolding. This step is called purification and typically involves applying the solution containing the refolded protein to a "separation matrix." Generally, the separation matrix can function in one of two ways. In "flow-through" purification the separation matrix attracts one or more of the unwanted chemicals used to solubilize and refold the protein. The protein itself,

however, does not attach to the matrix and thus "flows through" and is collected. By contrast, in "capture purification" the separation matrix attracts and binds *the protein* so that the unwanted contaminants and chemicals flow through the matrix and are discarded. The purified protein is then eluted (i.e., released) from the separation matrix and collected.

The present dispute between Amgen and Sandoz began in 2014. Over the past three years, the litigation between the parties has involved multiple issues and multiple patents. The only patent that remains at issue, however, is U.S. Patent No. 8,940,878 ("the '878 patent"), entitled "Capture Purification Processes for Proteins Expressed in a Non-Mammalian System." As the name suggests, the '878 patent generally relates to processes for purifying proteins. Claim 7 of the patent claims one such method. Amgen asserts that one of the steps in Sandoz's process for making and purifying filgrastim and pegfilgrastim ("the AEX step") infringes claim 7. Sandoz contends the AEX step does not infringe because it does not satisfy elements (e), (f) and (g) of claim 7:

> (e) directly applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix;
> (f) washing the separation matrix; and
> (g) eluting the protein from the separation matrix, wherein the separation matrix is a non-affinity resin selected from the group consisting of ion exchange, mixed mode, and a hydrophobic interaction resin.

While Amgen Inc. retains ownership of the '878 patent, Amgen Manufacturing Limited ("AML") is responsible for manufacturing Neupogen and Neulasta. AML does not practice the '878 patent method in manufacturing either product.[2]

III. LEGAL STANDARD

Summary judgment is proper "if the pleadings and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(c). The purpose of summary

[2] Additional background information regarding how recombinant proteins are genetically engineered and purified can be found in the claim construction order (14-cv-04741, Dkt. No. 205).

judgment "is to isolate and dispose of factually unsupported claims or defenses." *Celotex v. Catrett*, 477 U.S. 317, 323-24 (1986). The moving party "always bears the initial responsibility of informing the district court of the basis for its motion, and identifying those portions of the pleadings and admissions on file, together with the affidavits, if any, which it believes demonstrate the absence of a genuine issue of material fact." *Id*. at 323 (citations and internal quotation marks omitted). If it meets this burden, the moving party is then entitled to judgment as a matter of law when the non-moving party fails to make a sufficient showing on an essential element of the case with respect to which he bears the burden of proof at trial. *Id*. at 322-23.

The non-moving party "must set forth specific facts showing that there is a genuine issue for trial." Fed. R. Civ. P. 56(e). The non-moving party cannot defeat the moving party's properly supported motion for summary judgment simply by alleging some factual dispute between the parties. To preclude the entry of summary judgment, the non-moving party must bring forth material facts, i.e., "facts that might affect the outcome of the suit under the governing law . . . . Factual disputes that are irrelevant or unnecessary will not be counted." *Anderson v. Liberty Lobby, Inc*., 477 U.S. 242, 247-48 (1986). The opposing party "must do more than simply show that there is some metaphysical doubt as to the material facts." *Matsushita Elec. Indus. Co. v. Zenith Radio*, 475 U.S. 574, 588 (1986).

The court must draw all reasonable inferences in favor of the non-moving party, including questions of credibility and of the weight to be accorded particular evidence. *Masson v. New Yorker Magazine, Inc*., 501 U.S. 496 (1991) (*citing Anderson*, 477 U.S. at 255); *Matsushita*, 475 U.S. at 588 (1986). It is the court's responsibility "to determine whether the 'specific facts' set forth by the nonmoving party, coupled with undisputed background or contextual facts, are such that a rational or reasonable jury might return a verdict in its favor based on that evidence." *T.W. Elec. Service v. Pacific Elec. Contractors*, 809 F.2d 626, 631 (9th Cir. 1987). "[S]ummary judgment will not lie if the dispute about a material fact is 'genuine,' that is, if the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Anderson*, 477 U.S. at 248. However, "[w]here the record taken as a whole could not lead a rational trier of fact to find for the

non-moving party, there is no 'genuine issue for trial.'" *Matsushita*, 475 U.S. at 587.

IV. DISCUSSION

A. Noninfringement

Evaluating infringement is a two-part inquiry: 1) claim construction; and 2) comparison of the properly construed claims to the accused process. *Lockheed Martin Corp. v. Space Sys./Loral, Inc.*, 324 F.3d 1308, 1318 (Fed. Cir. 2003). In the instant case, part one of the inquiry was completed with issuance of the claim construction order on August 4, 2016. Part two is the subject of the present motion.

"[A] determination of infringement, both literal and under the doctrine of equivalents, is a question of fact." *Id.* Because the ultimate burden of proving infringement rests with the patentee, an accused infringer may show that summary judgment of non-infringement is proper either by producing evidence that would preclude a finding of infringement, or by showing that the evidence on file fails to create a material factual dispute as to any essential element of the patentee's case. *See Novartis Corp. v. Ben Venue Labs., Inc.*, 271 F.3d 1043, 1046 (Fed. Cir. 2001). Here, Sandoz can prevail only if no reasonable jury could conclude the accused AEX step infringes claim 7 of the '878 patent either literally or under the doctrine of equivalents.

i. Literal Infringement

To prove literal infringement, a patent holder must establish that every requirement of the claimed method is included in the method accused of infringement. *MicroStrategy Inc. v. Business Objects, S.A.*, 429 F.3d 1344, 1353 (Fed. Cir. 2005). "If . . . even one claim limitation is missing or not met, there is no literal infringement." *Id.* at 1353 (citation omitted).

The overarching thrust of Sandoz's argument is that the claimed protein purification method requires three distinct and sequential steps as well as the application of three distinct solutions. Sandoz's AEX step, by contrast, involves only one step and only one solution. More specifically, Sandoz identifies four requirements of claim 7 it argues are not satisfied by its accused process. First, the eluting step must occur after the washing step. Second, the washing step must occur after direct application of the refold solution. Third and fourth, both the washing

and eluting steps require adding solutions different from the refold solution.

The first ground raised by Sandoz (i.e., that the eluting step must occur after the washing step) is sufficient on its own to support a finding that Sandoz's AEX step does not literally infringe the '878 patent. In construing the phrase "eluting the protein from the separation matrix," the claim construction order noted that the eluting step outlined in 7(g) must occur *after* the washing step described in 7(f). CC Order at 31, 33. This conclusion was reached in heavy reliance on the explicit language of the patent specification:

> The specification teaches, "[a]fter the separation matrix with which the protein has associated has been washed, the protein of interest is eluted using an appropriate solution." '878 Patent at 15:60 62. It further explains that the wash buffer may be comprised of any number of components so long as "[t]he pH range is chosen to optimize the chromatography conditions, preserve protein binding, and to retain the desired characteristics of the protein of interest." '878 Patent at 15:55 57 (emphasis added). Thus, the proteins and separation matrix should remain associated during the washing process. In contrast, elution involves cleaving the protein from the matrix with "a solution that interferes with the binding of the absorbent component of the separation matrix to the protein, for example by disrupting the interactions between Protein A and the Fc region of a protein of interest." '878 Patent at 15:65 16:2 (emphasis added). *Accordingly, the specification discloses a natural, logical order of steps. If the washing and eluting steps occurred simultaneously, the protein captured by the separation matrix could once again comingle with the contaminants and components to be washed away.* In light of the fact Amgen has not offered any reasons to believe the claim does not imply a natural order, the construction of the phrase will make clear the step of "eluting the protein from the separation matrix" occurs *after* the step of "washing the separation matrix."

Id. at 31 (emphasis added).

Nothing has been offered to suggest the above construction needs modification. Based on this construction, the method employed by Sandoz does not have the sequential washing and eluting steps required by claim 7. The AEX step entails continuously pumping a refold solution comprised of filgrastim, a particular detergent ("detergent 1"),[3] and other substances into a column containing a separation matrix. There is no pause in the pumping of the refold solution. Nor is there any point at which Sandoz adds a second solution to the column that is compositionally

[3] This nomenclature is adopted to avoid unnecessarily disclosing confidential aspects of Sandoz's accused process.

different than the refold. There simply is no way to conceive of this continuous pumping process as an eluting step *after* a washing step without straining the language of the patent specification and the claim construction order beyond their reasonable meaning.

Amgen nonetheless argues the washing and eluting steps *do occur* sequentially in Sandoz's process if you look at any given location in the column (e.g., "the leading edge of the refold solution in the downstream end") rather than at the column as a whole. The key, according to Amgen, is recognizing that conditions in the column are changing as the refold solution is applied. When the solution is first applied, conditions are such that filgrastim *is binding* to the separation matrix. While the filgrastim is bound, other contaminants in the solution are flowing over and past it through the column and being discarded (i.e., "washing"). Later, the continued application of refold solution causes conditions to change in the column yet again so that the filgrastim binding is reversed and the protein flows out through the column (i.e., "eluting"). Thus, Amgen argues, Sandoz's description of its AEX step as only one step and one solution is misleading. At any given location in the column where filgrastim binds, the washing step and the eluting step are occurring sequentially consistent with claim 7.

Amgen's attempt to redefine Sandoz's accused process in a way that fits the requirements of claim 7 is unavailing. As the claim construction order noted, the patent specification discloses a natural, logical order of steps. Nowhere is that order of steps more clear than with regard to the requirement that the eluting step in element (g) follow the washing step in element (f).

For similar reasons, Sandoz's argument that the washing and eluting solutions must be distinct is equally compelling and provides an additional ground on which to conclude that Sandoz's process does not literally infringe the claimed method. As previously discussed, Sandoz's AEX step uses only one solution. Yet the patent specification describes a "wash buffer" that is "optimized to preserve protein binding" and an eluting solution that "interferes with the binding." '878 Patent at 15:55-62. *See also* CC Order at 31. The opposite purposes of these two solutions suggests they must indeed be distinct, and cannot be, as Amgen contends, a single solution achieving different ends, due to different conditions, at different points in time.

Sandoz's other arguments—that the washing step must come after the application of the refold solution and that the solutions required for eluting and washing must be separate and distinct from the refold solution—are also strong. Those arguments, however, need not be reached. Eluting must follow washing under the claimed method. The accused AEX step has no such sub-steps. So too, the claimed method requires that the washing and elution solutions be distinct. Yet the accused AEX step involves application of only one solution. Either one of these grounds independently supports a finding that Sandoz's process does not literally infringe.

ii. Doctrine of Equivalents

An accused method that does not literally infringe a patent claim may still be found to be infringing under the doctrine of equivalents if it includes steps that are identical or equivalent to the requirements of the claim. *Warner–Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997). An accused step is considered equivalent to a claim requirement if a person of ordinary skill in the field would think that the differences between the step and the requirement were not substantial. *See Johnson & Johnston Assocs. Inc. v. R.E. Serv. Co.*, 285 F.3d 1046, 1057 (Fed. Cir. 2002). An accused step may be insufficiently different from a claim requirement if it performs substantially the same function, in substantially the same way, to achieve substantially the same result. *See Warner-Jenkinson Co.*, 520 U.S. at 39-40; *Graver Tank & Mfg. Co. v. Linde Air Products Co.*, 339 U.S. 605, 608 (1950). As the patentee, Amgen bears the burden of establishing equivalency on a limitation-by-limitation basis by particularized testimony and linking argument as to the insubstantiality of the differences between the claimed and accused methods. *Akzo Nobel Coatings, Inc. v. Dow Chem. Co.*, 811 F.3d 1334, 1342 (Fed. Cir. 2016).

Here, the differences between the method claimed by the '878 patent and the accused AEX step are substantial. First, the claimed method and the AEX step do not perform the same function. As explained in the claim construction order, the alleged invention protected by the '878 patent was the discovery that refold solution could be applied directly to a separation matrix without removing components of or diluting the solution. CC Order at 25. The AEX step, by removing an unwanted contaminant ("detergent 1") in advance of capture purification, is in effect doing exactly

what the asserted claims sought to eliminate.

Second, the different functions performed by the two processes are performed in substantially different ways. Sandoz argues this distinction is best illustrated by classifying the claimed method as a "capture purification" process and the accused method as "flow-through." Amgen rejects these classifications as misleading on the grounds that filgrastim actually does bind to at least some portion of the separation matrix during Sandoz's process and is therefore captured. Regardless of how they are labelled, however, the processes are indeed different. The claimed method "discloses a natural, logical order of steps" in which application of the refold solution is followed by a washing step and then an eluting step. The accused method, by contrast, involves only one step: the continuous application of a single solution to a separation matrix.

Lastly, and closely related to the function analysis above, the results produced by the claimed method and the accused method are substantially different. The claimed method, as the patent notes, is a "Capture Purification Process" that produces the protein in question in its purified form. There are no steps beyond the eluting step in element (g). The AEX step, on the other hand, produces a solution that contains the protein to be purified (filgrastim)—and at least one fewer contaminant ("detergent 1") than at the outset of the step—but which requires further purification.

In light of these differences, Amgen cannot prove infringement either literally or under the doctrine of equivalents. Sandoz's motion for summary judgment of noninfringement is granted.

B. Damages

In addition to seeking summary judgment as to noninfringement, Sandoz also moves for summary adjudication of several discrete issues impacting the scope of damages and relief available to Amgen. Specifically, Sandoz asks the Court to find: (1) AML lacks standing to sue for infringement because it is neither an owner nor exclusive licensee of the '878 patent; (2) Amgen Inc. is not entitled to lost profits for Neupogen, because it has never made or sold any Neupogen; (3) Amgen cannot prove the absence of non-infringing alternatives; and (4) the hypothetical negotiation date for determining royalties must be earlier than May 5, 2015. Because Sandoz's

accused method does not infringe the ’878 patent, these damages arguments need not be reached.

C. Rule 56(d) Motion

Rule 56(d) of the Federal Rules of Civil Procedure permits denial or continuance of a motion for summary judgment, “[i]f a nonmovant shows by affidavit or declaration that, for specified reasons, it cannot present facts essential to justify its opposition.” A party requesting a Rule 56(d) continuance bears the burden of setting forth specific facts he hopes to elicit from further discovery and demonstrating that the facts sought not only exist but also are essential to oppose summary judgment. *Family Home & Fin. Ctr., Inc. v. Fed. Home Loan Mortg. Corp.*, 525 F.3d 822, 827 (9th Cir. 2008). Failing to meet this burden “is grounds for the denial” of a Rule 56(d) motion. *Pfingston v. Ronan Eng. Co.*, 284 F.3d 999, 1005 (9th Cir. 2002).

As discussed previously, Sandoz’s accused AEX step involves pumping refold solution into a column containing a separation matrix. The specific matrix Sandoz currently uses, however, will be discontinued in late 2018 or 2019. Sandoz therefore plans to replace its current matrix with a new separation matrix. Amgen argues this change in matrices is significant and moves pursuant to Rule 56(d) to defer a ruling on whether Sandoz’s modified process infringes on the claimed method. Such a ruling is not appropriate, Amgen argues, until Sandoz produces more complete documentation regarding how the process will be modified. Specifically, Amgen urges the court to wait until Sandoz submits an application for approval of its modified process to the FDA—which will happen at some point in 2018—and produces that submission and its underlying source documents to Amgen.

The problem with Amgen’s request is that the final “process parameters” it hopes to discover (e.g., “column dimensions, flow rate, loading time, and residence time”) are not material to the finding of noninfringement. As discussed in the infringement analysis, the method claimed by the ’878 patent involves multiple steps and multiple solutions while Sandoz’s accused method involves only one continuous step and only one solution. This substantial difference between the methods will not be altered by the replacement of the current matrix with the new matrix. The core function of the new matrix, to capture “detergent 1” as the refold solution moves through the

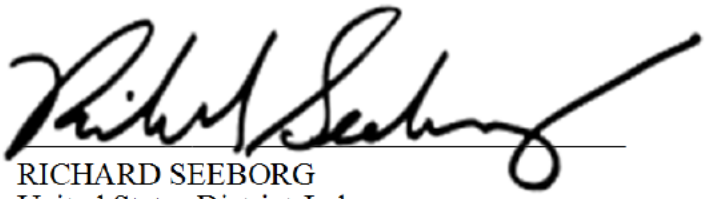
column, will be materially identical to the function of the current matrix. Sandoz's process will still not contain an eluting step that follows a washing step, as required by claim 7's (f) and (g) elements. It therefore will not infringe. Accordingly, granting Amgen's Rule 56(d) motion would not conserve judicial resources, as Amgen argues, but would instead unnecessarily delay resolution of this already lengthy litigation.

V. CONCLUSION

Sandoz's motion for summary judgment of noninfringement is granted with respect to its accused process as conducted with both the current and new separation matrices. Amgen's Rule 56(d) motion is denied. Sandoz's motion for summary judgment regarding damages is denied as moot. Sandoz is directed to submit a proposed final judgment no later than January 5, 2018.

IT IS SO ORDERED.

Dated: December 19, 2017



RICHARD SEEBORG
United States District Judge

United States District Court
Northern District of California