

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28

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.

1 **II. BACKGROUND**

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

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

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

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

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

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

20 While Amgen Inc. retains ownership of the ’878 patent, Amgen Manufacturing Limited
21 (“AML”) is responsible for manufacturing Neupogen and Neulasta. AML does not practice the
22 ’878 patent method in manufacturing either product.²

23 **III. LEGAL STANDARD**

24 Summary judgment is proper “if the pleadings and admissions on file, together with the
25 affidavits, if any, show that there is no genuine issue as to any material fact and that the moving
26 party is entitled to judgment as a matter of law.” Fed. R. Civ. P. 56(c). The purpose of summary
27

28 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).

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

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

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

1 non-moving party, there is no ‘genuine issue for trial.’” *Matsushita*, 475 U.S. at 587.

2 **IV. DISCUSSION**

3 **A. Noninfringement**

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

9 “[A] determination of infringement, both literal and under the doctrine of equivalents, is a
10 question of fact.” *Id.* Because the ultimate burden of proving infringement rests with the patentee,
11 an accused infringer may show that summary judgment of non-infringement is proper either by
12 producing evidence that would preclude a finding of infringement, or by showing that the
13 evidence on file fails to create a material factual dispute as to any essential element of the
14 patentee’s case. *See Novartis Corp. v. Ben Venue Labs., Inc.*, 271 F.3d 1043, 1046 (Fed. Cir.
15 2001). Here, Sandoz can prevail only if no reasonable jury could conclude the accused AEX step
16 infringes claim 7 of the ’878 patent either literally or under the doctrine of equivalents.

17 **i. Literal Infringement**

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

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

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

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

8 The specification teaches, “[a]fter the separation matrix with which the protein has
9 associated has been washed, the protein of interest is eluted using an appropriate solution.”
10 ’878 Patent at 15:60 62. It further explains that the wash buffer may be comprised of any
11 number of components so long as “[t]he pH range is chosen to optimize the
12 chromatography conditions, preserve protein binding, and to retain the desired
13 characteristics of the protein of interest.” ’878 Patent at 15:55 57 (emphasis added). Thus,
14 the proteins and separation matrix should remain associated during the washing process. In
15 contrast, elution involves cleaving the protein from the matrix with “a solution that
16 interferes with the binding of the absorbent component of the separation matrix to the
17 protein, for example by disrupting the interactions between Protein A and the Fc region of
18 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.”

18 *Id.* at 31 (emphasis added).

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

25
26 _____
27 ³ This nomenclature is adopted to avoid unnecessarily disclosing confidential aspects of Sandoz’s
28 accused process.

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

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

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

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

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

8 ii. Doctrine of Equivalents

9 An accused method that does not literally infringe a patent claim may still be found to be
10 infringing under the doctrine of equivalents if it includes steps that are identical or equivalent to
11 the requirements of the claim. *Warner–Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21
12 (1997). An accused step is considered equivalent to a claim requirement if a person of ordinary
13 skill in the field would think that the differences between the step and the requirement were not
14 substantial. *See Johnson & Johnston Assocs. Inc. v. R.E. Serv. Co.*, 285 F.3d 1046, 1057 (Fed. Cir.
15 2002). An accused step may be insufficiently different from a claim requirement if it performs
16 substantially the same function, in substantially the same way, to achieve substantially the same
17 result. *See Warner-Jenkinson Co.*, 520 U.S. at 39-40; *Graver Tank & Mfg. Co. v. Linde Air*
18 *Products Co.*, 339 U.S. 605, 608 (1950). As the patentee, Amgen bears the burden of establishing
19 equivalency on a limitation-by-limitation basis by particularized testimony and linking argument
20 as to the insubstantiality of the differences between the claimed and accused methods. *Akzo Nobel*
21 *Coatings, Inc. v. Dow Chem. Co.*, 811 F.3d 1334, 1342 (Fed. Cir. 2016).

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

1 what the asserted claims sought to eliminate.

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

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

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

20 **B. Damages**

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

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

2 **C. Rule 56(d) Motion**

3 Rule 56(d) of the Federal Rules of Civil Procedure permits denial or continuance of a
4 motion for summary judgment, “[i]f a nonmovant shows by affidavit or declaration that, for
5 specified reasons, it cannot present facts essential to justify its opposition.” A party requesting a
6 Rule 56(d) continuance bears the burden of setting forth specific facts he hopes to elicit from
7 further discovery and demonstrating that the facts sought not only exist but also are essential to
8 oppose summary judgment. *Family Home & Fin. Ctr., Inc. v. Fed. Home Loan Mortg. Corp.*, 525
9 F.3d 822, 827 (9th Cir. 2008). Failing to meet this burden “is grounds for the denial” of a Rule
10 56(d) motion. *Pfingston v. Ronan Eng. Co.*, 284 F.3d 999, 1005 (9th Cir. 2002).

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

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

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

6 **V. CONCLUSION**

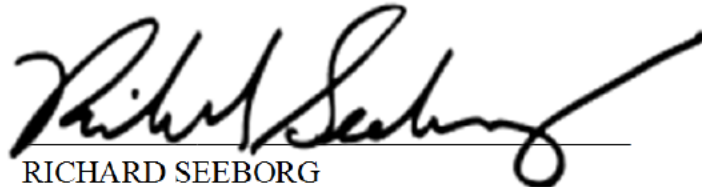
7 Sandoz's motion for summary judgment of noninfringement is granted with respect to its
8 accused process as conducted with both the current and new separation matrices. Amgen's Rule
9 56(d) motion is denied. Sandoz's motion for summary judgment regarding damages is denied as
10 moot. Sandoz is directed to submit a proposed final judgment no later than January 5, 2018.

11

12 **IT IS SO ORDERED.**

13

14 Dated: December 19, 2017



RICHARD SEEBORG
United States District Judge

15

16

17

18

19

20

21

22

23

24

25

26

27

28