IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

SPECTRUM PHARMACEUTICALS, INC. and UNIVERSITY OF STRATHCLYDE, Plaintiffs, v. INNOPHARMA, INC., MYLAN TEORANTA, MYLAN INSTITUTIONAL LLC, and MYLAN INSTITUTIONAL INC., Defendants.	)	Civil Action No. 12-260-RGA-CJB

REPORT AND RECOMMENDATION

In this action filed by Plaintiffs Spectrum Pharmaceuticals, Inc. ("Spectrum") and University of Strathclyde (collectively, "Plaintiffs") against Defendants InnoPharma, Inc. ("InnoPharma"), Mylan Teoranta, Mylan Institutional LLC and Mylan Institutional Inc. (the "Mylan Defendants" and, collectively with InnoPharma, "Defendants"), Plaintiffs allege infringement of U.S. Patent No. 6,500,829 (the "'829 patent"). Presently before the Court is the matter of claim construction. The Court recommends that the District Court adopt the constructions as set forth below.

I. BACKGROUND

A. The Asserted Patent

Plaintiffs assert infringement of the '829 patent, a patent entitled "Substantially Pure Diastereoisomers of Tetrahydrofolate Derivatives[.]" (D.I. 1, ex. A (hereinafter, the "'829 patent" or "the patent")) The patent is based on U.S. Appl. No. 08/426,458 and was issued on

December 31, 2002. (*Id.*) At the time of its issue, the '829 patent was assigned to University of Strathclyde, who subsequently issued an exclusive license to Spectrum. (D.I. 100 at ¶ 13)

The present invention centers on 5-formyltetrahydrofolic acid, a chemical compound commonly known as leucovorin. ('829 patent, col. 1:28-29) According to the '829 patent, leucovorin has long been used to act as a "rescue agent" to help prevent the toxic side effects of methotrexate, a chemotherapy agent. (*Id.*, col. 1:19-29; D.I. 47 at 2) The leucovorin compound is composed of equal amounts of two diastereoisomers, referred to as the "(6S)" and "(6R)" diastereoisomers. (D.I. 47 at 2; D.I. 52 at 1) The '829 patent asserts, however, that a report from 1981 found that only the (6S) diastereoisomer—also known as levoleucovorin—is responsible for leucovorin's beneficial clinical effects. ('829 patent, col. 1:57-61; *see also* D.I. 52 at 2) Other reports suggested that the (6R) diastereoisomer might actually inhibit the beneficial effects of the (6S) diastereoisomer. (*Id.*, cols. 1:62-2:12) Accordingly, the present invention relates to the preparation of a substantially pure form of the desired (6S) diastereoisomer from leucovorin. (*Id.*, Abstract; *id.*, Fig. 4; *see also* D.I. 52 at 3)

B. Procedural Posture

This case arises out of InnoPharma's submission of Abbreviated New Drug Application ("ANDA") No. 203576 to the United States Food and Drug Administration ("FDA"), which seeks to market levoleucovorin products that are generic forms of Fusilev®, Spectrum's pharmaceutical product. (D.I. 100 at ¶¶ 1, 19) Spectrum is the holder of approved New Drug Application No. 20-140, which covers Fusilev®. (*Id.* at ¶ 14)

Plaintiffs filed suit against InnoPharma on March 2, 2012, alleging that InnoPharma's submission of ANDA No. 203576 infringes at least one claim of the '829 patent under 35 U.S.C.

§ 271(e)(2)(A). (D.I. 1 at ¶ 22) Plaintiffs now make infringement allegations against InnoPharma and the three Mylan Defendants (who are said to have entered into an agreement to market InnoPharma's products at issue, or to be affiliated with entities that have done so), pursuant to 35 U.S.C. § 271(a)-(c).[1] (D.I. 100 at ¶¶ 7, 24, 28-31)

On May 23, 2012, this case was referred to the Court by Judge Richard G. Andrews to hear and resolve all pretrial matters, up to and including case-dispositive motions. The parties completed initial briefing on claim construction on June 28, 2013. (D.I. 74) This briefing was followed by a series of letters to the Court from the parties further addressing the disputed claim terms. (D.I. 80, 82, 83, 84) The Court held a *Markman* hearing on July 23, 2013. (July 23, 2013 Hearing Transcript, hereinafter "Tr.") Pursuant to the Court's request at that hearing, (Tr. at 5), the parties later filed a joint stipulation requesting that the Court adopt agreed-upon constructions of nine terms in the '829 patent that had earlier been the subject of disputes between them. (D.I. 85)

After the *Markman* hearing, Plaintiffs submitted a notice of subsequent authority, attaching a Claim Construction Order issued by the United States District Court for the District of Nevada, *Spectrum Pharms., Inc. v. Sandoz Inc.*, No. 2:12-cv-000111-GMN-NJK, 2013 WL 6865692 (D. Nev. Dec. 31, 2013) (hereinafter, the "Nevada Order"), which construed terms of the '829 patent that are at issue in this case. (D.I. 109) Each side later submitted a letter to the Court addressing whether one of the constructions found in the Nevada Order should be adopted by this Court. (D.I. 110, 117) The Court then held a hearing on February 14, 2014, where it

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[1] On December 9, 2013, Plaintiffs amended their Complaint to name the three Mylan Defendants as Defendants in the case. (D.I. 100)

allowed the parties to make supplemental *Markman* presentations in light of the Nevada Order. (D.I. 164, ex. 3)

After a discovery dispute arose, (*see* D.I. 141), the parties asked the Court to construe one additional term of the '829 patent, (D.I. 158). The parties submitted briefing on this additional term, and completed such briefing on May 12, 2014. (D.I. 172)

II. STANDARD OF REVIEW

It is well-understood that "[a] claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using, or selling the protected invention." *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989). The proper construction of claim terms is a question of law for the Court. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). The Court should generally give claim terms their "'ordinary and customary meaning[,]'" which is "the meaning that the term[s] would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (citations omitted). However, when determining the ordinary meaning of claim terms, the Court should not extract and isolate those terms from the context of the patent, but rather should endeavor to reflect their "meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321.

To that end, the Court should look first and foremost to the language of the claims, because "[i]t is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Id.* at 1312 (internal quotation marks and citations omitted). For example, the context in which a term is used in a claim may be "highly

instructive." *Id.* at 1314. In addition, "[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable" in discerning the meaning of a particular claim term. *Id.* This is "[b]ecause claim terms are normally used consistently throughout the patent, [and so] the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Id.* Moreover, "[d]ifferences among claims can also be a useful guide," as when "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15.

In addition to the words of the claims, the Court should look to other intrinsic evidence. For example, the Court should analyze the patent specification, which "may reveal a special definition given to a claim term . . . that differs from the meaning [that term] would otherwise possess." *Id.* at 1316. In that case, "the inventor's lexicography governs." *Id.* Even if the specification does not contain a special definition of the term at issue, it "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Id.* at 1315 (internal quotation marks and citation omitted). That said, however, the specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004). In addition to the specification, a court should also consider the patent's prosecution history, if it is in evidence, because it "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention[.]" *Phillips*, 415 F.3d at 1317 (citations omitted).

Extrinsic evidence, "including expert and inventor testimony, dictionaries, and learned treatises[,]" can also "shed useful light on the relevant art." *Id.* (internal quotation marks and

citations omitted). Dictionaries (especially technical dictionaries) may be useful in this process because they typically provide "the accepted meanings of terms used in various fields of science and technology[.]" *Id.* at 1318. However, the United States Court of Appeals for the Federal Circuit has cautioned that "heavy reliance on [a] dictionary divorced from the intrinsic evidence risks transforming the meaning of the claim term to the artisan into the meaning of the term in the abstract, out of its particular context, which is the specification." *Id.* at 1321. Overall, while extrinsic evidence may be useful, it is "less significant than the intrinsic record in determining the legally operative meaning of claim language." *Id.* at 1317 (internal quotation marks and citations omitted); *accord Markman*, 52 F.3d at 981.

In utilizing these resources during claim construction, courts should keep in mind that "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998).

III. DISCUSSION

A. Agreed Constructions

As noted above, the parties have reached agreement with respect to construction of nine claim terms in the '829 patent that were previously in dispute. (*See* D.I. 85) The Court recommends that these now agreed-upon constructions be adopted, and includes the parties' agreed-upon constructions as part of the Court's recommended constructions (listed as constructions 1-9) at the conclusion of this Report and Recommendation. *Research Found. of State Univ. of N.Y. v. Mylan Pharms., L.P.*, C.A. No. 09-184-JJF-LPS, 2010 WL 1911589, at *2 (D. Del. May 12, 2010).

B. Disputed Terms

1. The "mixture" and "percentage" claim terms

The first dispute concerns two sets of claim terms, those labeled by Defendants as the "mixture" and "percentage" claim terms. The "mixture" claim terms are: "the compound consists of a mixture of (6S) and (6R) diastereoisomers" (found in Claim 1); "the composition consists of a mixture of (6S) and (6R) diastereoisomers" (found in Claim 5); and "a mixture of: a (6S) diastereoisomer selected from the group consisting of (6S) leucovorin (5-formyl-(6S)-tetrahydrofolic acid) and pharmaceutically acceptable salts and esters of (6S) leucovorin and the (6R) diastereoisomer thereof" (found in Claim 10). (D.I. 47 at 5-6; D.I. 52, ex. A) The "percentage" claim terms are: "consists of at least 92% by weight of the (6S) diastereoisomer" (found in Claim 1); "which consists of greater than 95% by weight of the (6S) diastereoisomer" (found in Claim 2); "consists of at least about 92% by weight of the (6S) diastereoisomer" (found in Claim 5); "said mixture of (6S) and (6R) diastereoisomers consists of at least about 95% by weight of the (6S) diastereoisomer" (found in Claim 7); "said mixture of (6S) and (6R) diastereoisomers consists of at least about 92% by weight of the (6S) diastereoisomer" (found in Claim 10); and "said mixture of (6S) and (6R) diastereoisomers consists of at least about 95% by weight of the (6S) diastereoisomer" (found in Claim 12). (D.I. 47 at 11-12; D.I. 52, ex. A)

As noted above, the "mixture" and "percentage" terms are found in Claims 1, 2, 5, 7, 10 and 12 of the '829 patent, respectively. (D.I. 47 at 5-6, 11-12) Moreover, the two sets of terms are related to each other, in that the compositions referred to in the "mixture" terms in Claims 1, 5, and 10 are said to "consist[] of" what is further described in the "percentage" terms in Claims 1, 2, 5, 7, 10 and 12. Claim 1's language is representative (at least for purposes of the dispute

here) of the way the terms are used in other of the patent's claims:

> A pharmaceutical composition for therapeutic use which consists essentially of a therapeutically effective amount sufficient for the treatment of human beings for methotrexate rescue or folate deficiency, of a pharmaceutically acceptable compound which is a (6S) diastereoisomer selected from the group consisting of (6S) leucovorin (5-formyl-(6S)-tetrahydrofolic acid) and pharmaceutically acceptable salts and esters of (6S) leucovorin; wherein *the compound consists of a mixture of (6S) and (6R) diastereoisomers* and *consists of at least 92% by weight of the (6S) diastereoisomer*, the balance of said compound consisting of the (6R) diastereoisomer; in combination with a pharmaceutically acceptable carrier.

('829 patent, col. 9:55-67 (emphasis added))

The parties initially briefed these two sets of terms separately, (D.I. 47, 52); however, they now agree that their dispute as to both term sets in fact relates to a single, common issue: whether there is an upper limit on the purity of the composition recited in the claims as including no more than 98% (6S) diastereoisomer by weight. (D.I. 72 at 1-2; Tr. at 9-10, 55) Defendants propose that the claim terms be construed to require an upper limit of 98% (6S) diastereoisomer by weight; in doing so, and in attempting to make that requirement clear, they have now focused particularly on the constructions that they put forward regarding the "percentage" terms. (D.I. 47 at 12; D.I. 72 at 2)[2] In Claim 1, for example, Defendants propose that the "percentage" term at issue ("consists of at least 92% by weight of the (6S) diastereoisomer") should be construed to mean "consists of (6S) diastereoisomer having a diastereoisomeric purity of 92% by weight up to 98% by weight[.]" (D.I. 47 at 11) As to the other "percentage" claim terms (in Claims 2, 5, 7,

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[2] For that reason, when the Court addresses Defendants' proposed constructions, it will focus on the constructions it previously put forward with regard to the "percentage" terms only.

10 and 12, respectively), the terms state that composition consists of "at least about" or "greater than" some percentage of (6S) diastereoisomer. (*Id.* at 11-12; D.I. 52, ex. A at 1-2) As to those terms, in each instance, Defendants propose that the proper construction requires that the percentage of (6S) diastereoisomer be no greater than 98%. (*Id.*)

For their part, while Plaintiffs have proposed constructions for each of these claim terms, (D.I. 52, ex. A), they acknowledge that the import of their proposals is essentially to argue that the plain and ordinary meaning of the terms should control. (Tr. at 11-13) That is, Plaintiffs believe that the claim terms' meaning reflect no 98% upper limit on the percentage of (6S) diastereoisomer. (*Id.*)

a. The claim language

In resolving this dispute, the Court looks first to the claim language itself. As noted above, in the relevant claims, the composition at issue is noted as consisting of "at least[,]" "greater than" or "at least about" some percentage of (6S) diastereoisomer. (D.I. 52, ex. A at 1-2) The Federal Circuit has found that the ordinary meaning of such phrases indicates an "open-ended range" starting at (or in the case of "at least about[,]" slightly below) the numerical value in the claim. *Quantum Corp. v. Rodime, PLC*, 65 F.3d 1577, 1581-82 (Fed. Cir. 1995); *see also Rowpar Pharms. Inc. v. Lornamead Inc.*, No. CV-13-01071-PHX-DGC, 2014 WL 1259777, at *11 (D. Ariz. Mar. 25, 2014) (finding that "the ordinary meaning of 'at least' sets a lower limit on the claimed range but says nothing about the upper limit"); *Astrazeneca AB, v. Dr. Reddy's Labs., Ltd.*, Civil Action No. 05-5553 (JAP), 2010 WL 1981790, at *4 (D.N.J. May 18, 2010) (holding that the ordinary and customary meaning of the term "at least about" is "equal to or more than approximately") (internal quotation marks omitted).

Defendants argue that the "more limited percentage ranges" in unasserted claims dependent on Claim 1 evidence an intention by the patentee to claim compositions no greater than 98% (6S) diastereoisomer. (D.I. 47 at 13) These dependant, unasserted claims—Claims 3 and 4—state that the percentage of (6S) diastereoisomer by weight is "about 92%" and "essentially . . . 92% to 95%[,]" respectively. ('829 patent, col. 10:4-8) Contrary to Defendants' argument, in the Court's view, the presence of these restrictions in other claims of the '829 patent indicates that "when the inventor wanted to restrict [] claims . . . , he did so explicitly." *Kara Tech. Inc. v. Stamps.com Inc.*, 582 F.3d 1341, 1347 (Fed. Cir. 2009). Accordingly, the claim language does not provide reason to impose an upper limit of 98% (6S) diastereoisomer by weight, and indeed suggests that no such upper limit was contemplated. *Accord Spectrum Pharms., Inc.*, 2013 WL 6865692, at *9.

b. The specification

The specification of the '829 patent supports a broad reading of the claim terms. It teaches three specified "standard techniques" to separate isomers, and thus achieve greater percentages of the (6S) diastereoisomer. ('829 patent, col. 3:42-58) By carrying out these techniques "repeated[ly][,]" one can "improve purity." (*Id.*, col. 3:53-58) The specification does not explicitly or implicitly suggest that any upper limit on the percentage of the (6S) diastereoisomer would result from such "repeated" use of these techniques. (*Id.*) Indeed, in describing the present invention as one that "provides substantially pure diastereoisomers[,]" and defining "substantially pure" as "most preferably greater than 95%[,]" the specification suggests just the opposite. (*Id.*, col. 4:25-30)

Although the specification does not explicitly reference an upper limit of 98% (6S)

diastereoisomer by weight (and indeed does not mention a "98%" figure in any context), Defendants argue that it nevertheless "provides guidance" in support of their proposed construction. (D.I. 47 at 12-13) This is so, they argue, because the specification never "describe[s] performing successive separation steps resulting in purities above 98%." (*Id.*) Defendants explicitly rely on Example 1 of the '829 patent, an example of the solvent extraction technique, which yields mixtures with 91% and 92% isometric purity. (*Id.* at 12 (citing '829 patent, col. 6:51-56); D.I. 52 at 13) The Federal Circuit, however, has warned against confining the claims of a patent to specific embodiments described in the specification. *See Phillips*, 415 F.3d at 1323 (importing limitations from the specification into the claims should be avoided unless the patentee clearly "intends for the claims and the embodiments in the specification to be strictly coextensive"); *accord Spectrum Pharms., Inc.*, 2013 WL 6865692, at *9. Furthermore, as Plaintiffs note, (D.I. 52 at 13), the solvent extraction technique used in Example 1 amounts to only one of the three "standard techniques" listed in the patent used to separate the isomers. And in any event, the specification itself states that the examples provided merely "serve to illustrate the invention in a non-limiting manner[.]" ('829 patent, col. 5:31-32)

Accordingly, the Court finds that the specification supports the broader reading of the claim terms proposed by Plaintiffs.[3] *See Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, 457 F.3d 1284, 1290

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[3] At the *Markman* hearing, Defendants put forward an additional argument not raised in their earlier briefing, which also appears to be based on the content of the '829 patent's specification. In essence, this new argument is as follows: (1) the '829 patent promotes two objectives: "getting reasonable purity in reasonable yield"; (2) these two objectives are in tension with one another, such that when one obtains greater purity, one obtains a smaller yield; and (3) because the desired yield must only be "reasonable," and because the desired purity need only be "reasonable," some level of purity above 90% was all that the applicants "needed." (Tr. at 79–81) Even assuming *arguendo* that Defendants are correct that obtaining only reasonable purity and a reasonable yield are the two prime objectives of the patent (and the Court is not

(Fed. Cir. 2006) (affirming the district court's decision not to restrict claim language to an example provided in the specification, particularly because the specification stated that "[t]he[] examples are illustrative and are not to be read as limiting the scope of the invention as it is defined by the appended claims") (internal quotation marks omitted).

c. Prosecution disclaimer

Defendants also address two elements of the prosecution history, each of which, they argue, constitutes prosecution disclaimer. As previously noted above, the Federal Circuit has stated that "the prosecution history can often inform the meaning of the claim language by demonstrating . . . whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Phillips*, 415 F.3d at 1317. Only a "clear and unmistakable" disavowal during prosecution overcomes the "'heavy presumption' that claim terms carry their full ordinary and customary meaning[.]" *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1323, 1326 (Fed. Cir. 2003) (quoting *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002)). The Court will address both of Defendants' arguments in turn.

(1) The Suckling Declaration

Defendants first point to the sworn declaration of co-inventor Dr. Colin James Suckling (the "Suckling Declaration"), a declaration filed along with the applicants' Reply Brief to the

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necessarily convinced that this is an accurate way of articulating the patent's objectives), there is no requirement that any one claim has to encompass *both* of these requirements. *See Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 908 (Fed. Cir. 2004) ("The fact that a patent asserts that an invention achieves several objectives does not require that each of the claims be construed as limited to structures that are capable of achieving all of the objectives."). Thus, even considering this new argument, the Court is not persuaded that an upper limit of 98% (6S) diastereoisomer by weight is appropriate in light of the specification.

United States Patent and Trademark Office (the "PTO") after the Examiner had rejected the claims for failure to enable preparation of mixtures of greater than 95% (6S) diastereoisomer by weight. (D.I. 47 at 14; *see also* D.I. 31-4 at 15) In that Declaration, Dr. Suckling submitted evidence of (6S) diastereoisomer (allowing for a rate of intrinsic error) that is "in the range of about 90-98%." (D.I. 49, ex. 1 at SPPI_INNO0000482) Defendants point to this statement, particularly its reference to a 98% figure, and argue that because the "declaration[] establish[es] that [this was] the highest purity of (6S) diastereoisomer achieved by the inventors[,]" Plaintiffs are "not entitled to a construction that provides a purity of (6S) diastereoisomer any higher than 98%."[4] (D.I. 47 at 14)

While it is true that the PTO did not receive data from the applicants showing that the invention achieved mixtures containing greater than 98% (6S) diastereoisomer by weight,[5] the

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[4] In their initial briefing, it was not clear that Defendants intended to argue that the applicants' submission of the Suckling Declaration amounted to prosecution disclaimer. (*See* D.I. 47 at 13-14 (Defendants arguing only that the Suckling Declaration "shed[s] light" on the "scope [and meaning] of the claims" in a manner consistent with their proposed constructions)) In their supplemental *Markman* presentation, however, it became clear that Defendants were arguing that the Suckling Declaration clearly disclaimed purities above 98%. (*See, e.g.*, D.I. 164, ex. 3 at 88 (Defendants' counsel arguing that purities above 98% are "disclaimed" here because they are "beyond what [the applicants] have argued was enabled" in the Suckling Declaration))

[5] Although it is clear that the *PTO did not receive* evidence of the invention achieving mixtures greater than 98% (6S) diastereoisomer by weight, the parties disputed whether Dr. Suckling had data at the time of the Suckling Declaration demonstrating (6S) diastereoisomer purity of greater than 98%. (*See* D.I. 97 at 2) Whether or not Dr. Suckling achieved such purity levels at that time does not affect the Court's conclusion here. This is so because, as explained herein, it appears that the applicants' goal in submitting the Suckling Declaration was to respond to the Examiner's statements regarding enablement, not to make a statement as to what was the highest possible purity level that had been or could be achieved. Indeed, Dr. Suckling's deposition testimony confirms this understanding. (*See* D.I. 117, ex. A at 60-61 (Dr. Suckling testifying that achieving (6S) diastereoisomer purity of greater than 98% "[w]ould not have been significant" because "the nature of the method would allow us to repeat the process and improve the diastereoisomeric purity simply by . . . doing it a few more times"))

words of the Suckling Declaration and related documents counsel against a conclusion that prosecution disclaimer occurred here. In summarizing the data presented, the Suckling Declaration states that "the (6S) leucovorin produceable according to the present invention is fairly characterized as being *at least 95%* (the balance being the (6R) diastereoisomer)." (D.I. 49, ex. 1 at SPPI_INNO0000482 (emphasis added)) This language, however, has to be read in the context of the applicants' letter to the PTO (that attached the Suckling Declaration itself). That letter stated that the applicant's primary purpose in submitting the Declaration was to "respond[] to" prior statements of the Examiner, who had noted "that the [applicants] would not state under oath that the specification is enabling to purities . . . above 95%" and "that Applicants did not file evidence that 95% or greater purity can be achieved by the present invention[.]" (*Id.* at SPPI_INNO0000477) In this context, Dr. Suckling's Declaration stating that the amount of (6S) leucovorin produceable according to the present invention is "at least 95%" does not appear at all intended to assert an *upper limit* on isomeric purity. Instead, it appears focused simply on providing proof, in response to the Examiner's challenge, that the applicants had achieved sufficient diastereoisomeric purity to meet the Examiner's proffered 95% hurdle.[6]

That this conclusion is correct is made even clearer by the content of the applicants'

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[6] Defendants also point to one other statement in the Suckling Declaration in support of their position here: a statement that the Declaration "presents further data which demonstrates that even higher diastereoisomeric purities of *up to and including* 95% are in fact attainable by the present invention." (D.I. 49, ex. 1 at "SPPI_INNO0000480" (emphasis added) (cited in D.I. 47 at 14)) The Court similarly finds that this statement does not do the work Defendants require of it. It is true that, in a vacuum, the "up to and including" language might be read as a reference to an upper limit on isomeric purity. Again, however, in light of the context of the entire submission, Dr. Suckling's use of the 95% figure here appears meant only to confirm to the Examiner that 95% purity is attainable by the present invention, without making a commentary one way or the other on whether greater purities are also attainable. Indeed, in other paragraphs of the Declaration, Dr. Suckling suggests that they are.

initial Appeal Brief to the PTO. In this brief, the applicants strenuously argued that, although an earlier-submitted declaration from Dr. Suckling contained data showing only 92% (6S) diastereoisomer by weight, one should not conclude that the invention was enabled only to that 92% level. (D.I. 31-4 at 18-22) Indeed, the applicants stated that there is "no basis in law, logic, or fact . . . support[ing] [the] conclusion" that the invention is enabled only to the uppermost purity of that submitted data. (*Id.* at 20) The applicants went on to argue that the Examiner's "inference" of non-enablement above 92% was "inappropriate" for numerous reasons. (*Id.*) Notably, the applicants asserted that the invention's steps can be repeated to increase purity, and stated that the specification explains how purity levels "greater than 95%" can be achieved. (*Id.* at 20-21)

Finally, at the supplemental *Markman* hearing, Defendants argued at length regarding how a 2013 Federal Circuit decision, *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090 (Fed. Cir. 2013), compels a finding in favor of their proposed construction. (*See, e.g.*, D.I. 164, ex. 3 at 61-72, 82-88; *see also* D.I. 117 at 4) Defendants are correct that in *Biogen*, as was the case here, the applicant's claims were rejected because the Examiner determined that the specification did not enable the full scope of the claims. *Biogen*, 713 F.3d at 1095-96. When confronted with this rejection, however, the applicant in *Biogen* did not challenge the Examiner's previously-stated understanding that the specification only enabled a portion of the fullest possible claim scope. *Id.* Instead, that applicant "conceded" that the Examiner's understanding was correct and "limited their claims" accordingly. *Id.* at 1096.[7] Here however, the applicants

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[7] *See also Biogen*, 713 F.3d at 1093, 1096 (noting that after the Examiner "acknowledged that the specification was enabling for Rituxan®, but that it was 'silent concerning what sort of specificity and affinity would be necessary' for other anti-CD20

made no such clear concession, for the reasons stated above. (*See also* D.I. 164, ex. 3 at 93-96, 107-08) Rather than agreeing with the Examiner that the invention was not enabled above 95% (6S) diastereoisomeric purity, the applicants argued vigorously to the contrary—and in doing so, did not clearly assert, as Defendants suggest, that "the claim scope of these claims stopped at 98 percent." (*Id.* at 64) Ultimately, the Examiner allowed the broad claim language the applicants pursued, the same language that is now at issue in this claim construction dispute.

Accordingly, the Court finds that the applicants' submission of the Suckling Declaration does not amount to a "clear and unmistakable" disavowal sufficient to overcome the "heavy presumption" that the claim terms here "carry their full ordinary and customary meaning." *Omega Eng'g, Inc.*, 334 F.3d at 1323, 1326 (internal quotation marks and citation omitted); *accord Spectrum Pharms., Inc.*, 2013 WL 6865692, at *9.

(2) Rees 1986

Defendants next argue that because the applicants disclaimed Rees 1986, a prior art reference, the applicants "necessarily disclaimed . . . (6S) diastereoisomer purity [of greater than] 98% by weight." (D.I. 47 at 15) Again, the Court disagrees.

Rees 1986 describes the synthesis of tetrahydrofolate derivatives, including (6S) leucovorin. (Declaration of Joe P. Foley, Ph.D. ("Foley Dec."), D.I. 48 at ¶ 35) It is not seriously disputed by either party that the limited language in Rees 1986 addressing leucovorin states that a "single peak[,]" and thus only a single product, i.e., the (6S) diastereoisomer, was

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antibodies[,]" the applicant responded by pointing to its disclosure of Rituxan® and arguing that the specification "was enabling for anti-CD20 antibodies with similar affinity and specificity as Rituxan®[,]" and thus, was "limiting the[] invention to what the examiner believed they enabled: antibodies that have a similar specificity and affinity for the specific epitope to which Rituxan® binds") (citations omitted).

formed. (*See* D.I. 52 at 20 (citing D.I. 54, ex. A at 118)) The Examiner for the '829 patent, however, rejected certain claims as anticipated by Rees 1986, relying primarily on earlier submissions from the applicants that it believed to have suggested that (6R) diastereoisomer is present in the resulting product taught by Rees 1986. (*See* D.I. 31-4 at 59) In their appeal to the PTO, the applicants clearly disputed the conclusion that Rees 1986 was addressing a mixture of (6S) and (6R) diastereoisomers, and also clearly disputed the Examiner's assertion that they had ever argued to the contrary.[8] (*See id.* at 34-35 (applicants arguing that Rees 1986 "did not make mixtures of (6S) and (6R) diastereoisomers, as specified in all claims of this case; but instead, prepared only the (6S) diastereoisomer"); *id.* at 89 (applicants addressing their earlier interpretations of Rees 1986, and stating that "no (6R) isomer was ever said to [have been] produced")) In sum, there is nothing in the prosecution history of the '829 patent regarding Rees 1986 that leads to the conclusion that the applicants clearly disclaimed (6S) diastereoisomeric purity of greater than 98% by weight—since in the relevant portions of the prosecution history where the applicant discussed Rees 1986, it was not asserting that this piece of prior art referenced a *mixture* of (6S) and (6R) diastereoisomers at all.

Rather than looking to the language of Rees 1986 or the prosecution history of the '829 patent, Defendants' prosecution disclaimer argument most particularly focuses on extrinsic evidence, namely the Declaration of Joe P. Foley, Ph.D. (D.I. 47 at 15; Foley Dec. at ¶¶ 34-59) Dr. Foley, a chemistry professor, concludes that a person of ordinary skill in the art would have

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[8] Even assuming for the sake of argument that, as Defendants suggest, the applicants *had* made an arguably contrary statement about Rees 1986 in an earlier submission, even Defendants concede that such an earlier statement would not amount to prosecution disclaimer here. (*See* Tr. at 97)

understood (even if the applicant did not describe the article to the PTO this way) that the product described in Rees 1986 contained "1% to 2% by weight (6R) diastereoisomer."[9] (Foley Dec. at ¶ 59 (emphasis omitted)) This conclusion is based on Dr. Foley's *own* evaluation of "the products described in Rees 1986[.]" (*Id.* at ¶ 42) In his evaluation, Dr. Foley "reproduced the chromatogram" from Rees 1986 and then performed several different methods to arrive at his conclusion as to what that chromatogram actually provides. (*Id.* at ¶¶ 42-55)

The Court, however, agrees with Plaintiffs that Defendants "cannot establish a 'clear and unmistakable' disclaimer of claim scope under the doctrine of prosecution disclaimer by relying on an expert's interpretation . . . of the data in Rees 1986, to conclude [that] Rees 1986 made a 98% pure product." (D.I. 52 at 21; *see also* D.I. 74 at 13-14) The issue as to prosecution disclaimer here is not what Dr. Foley now (rightly or wrongly) believes that the data in Rees 1986 demonstrates, but what *the applicant communicated to the PTO* about what the data in Rees 1986 demonstrates—and how any such statements might be credibly said to limit the scope of the applicable claims. On that score, even Dr. Foley acknowledges that the applicants asserted to the PTO that Rees 1986 disclosed "pure" (6S) diastereoisomer. (Foley Dec. at ¶ 36) Thus, Dr. Foley's conclusions about Rees 1986 do not support a prosecution history disclaimer argument, nor do they otherwise impact the Court's overall decision here. *Accord Spectrum Pharms., Inc.*, 2013 WL 6865692, at *10.

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[9] Dr. Foley also noted other publications made by the authors of Rees 1986 prior to that publication and concluded that, in light of those publications, "a person of ordinary skill in the art would have understood that the . . . (6S) diastereoisomer composition disclosed in Rees 1986 had a purity of 95% or higher." (Foley Dec. at ¶¶ 38-41) This conclusion, however, fails to address the crux of Defendants' prosecution disclaimer argument because it says nothing about the presence of (6R) diastereoisomer and does not place an upper limit on the purity of (6S) diastereoisomer.

(3) Conclusion as to prosecution disclaimer

In light of the conclusions set out above, the Court does not find Defendants' prosecution disclaimer arguments to have merit.

d. Defendants' other arguments

Defendants present two other arguments, each of which is based on their allegation that Plaintiffs' proposed construction does not draw a sufficiently clear line between the invention and pure (6S) diastereoisomer. First, Defendants argue that the Court should adopt their proposed claim construction imposing a 98% upper limit on (6S) diastereoisomeric purity, because failure to do so would impermissibly provide patent protection to a product of nature, in violation of Section 101 of the Patent Act and the Supreme Court of the United States' decision in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2116 (2013). (D.I. 72 at 7-9) Second, Defendants suggest that adoption of Plaintiffs' proposed claim constructions would render the patent invalid for indefiniteness under the new "reasonable certainty" standard set by the United States Supreme Court in *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120 (2014). (D.I. 175)

The Federal Circuit has stated that "validity analysis" is not "a regular component of claim construction." *Phillips*, 415 F.3d at 1327. Only if a court "concludes, after applying all the available tools of claim construction," that a claim is "ambiguous[,]" should it analyze whether a certain construction is necessary to sustain the claim's validity. *Id.* (internal quotation marks and citations omitted); *see also id.* at 1328 (asserting that the doctrine of construing claims to preserve their validity, is one "of limited utility"). Each of Defendants' two lines of argument is, in reality, centered on the patent's validity. *See, e.g.*, *Nautilus, Inc.*, 134 S. Ct. at 2124 ("In place

of the 'insolubly ambiguous' standard, we hold that a patent is *invalid for indefiniteness* if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention.") (emphasis added); *Ass'n for Molecular Pathology*, 133 S. Ct. at 2111 ("[W]e hold that a naturally occurring DNA segment is a product of nature and *not patent eligible* merely because it has been isolated, but that cDNA *is patent eligible* because it is not naturally occurring.) (emphasis added). However, the Court, for the reasons stated above, does not find the "mixture" and "percentage" claim terms at issue here to be "ambiguous." Thus, these terms "can be construed without the need to consider whether one possible construction would render the claim invalid while the other would not." *Phillips*, 415 F.3d at 1328.

Accordingly, the Court rejects Defendants' argument that a broad interpretation, along the lines of Plaintiffs' proposed construction, must be avoided because of concerns regarding indefiniteness or the patentability of a product of nature. *Cf. Merck & Co., Inc. v. Sun Pharm. Indus., Ltd.*, Civ. No. 12-5374 (FLW), 2014 WL 1691652, at *10-11 (D.N.J. Apr. 29, 2014) (following *Phillips* and finding that it would be inappropriate to construe a claim more narrowly based on the defendant's argument that a broad construction would render the asserted patent invalid for lack of enablement). The Court's decision as to construction of the terms at issue is without prejudice to Defendants' ability to challenge the validity of the claims at the summary judgment stage if they believe there is a basis to do so. *See, e.g., CSB-System Int't Inc. v. SAP Am., Inc.*, Civil Action No. 10-2156, 2011 WL 3240838, at *18 (E.D. Pa. July 28, 2011); *In re VTran Media Techs., LLC, Patent Litig.*, MDL Docket No. 1948, 2009 WL 2169155, at *11 & n.19 (E.D. Pa. July 17, 2009).

e. Conclusion

For the foregoing reasons, the Court declines to adopt Defendants' proposed construction that would add an unwarranted limitation to the terms at issue. With the Court having resolved that dispute, and because the meaning of the claim language in the terms is otherwise clear and unambiguous, the Court finds that the terms should be afforded their plain and ordinary meaning. *See Warner Chilcott Co., LLC v. Zydus Pharms. (USA) Inc.*, C.A. No. 11-1105-RGA, 2013 WL 1729383, at *3 (D. Del. Apr. 22, 2013) (finding no reason to read a "'boundary' limitation" into the disputed claim terms and adopting the plain and ordinary meaning of those terms); *accord Spectrum Pharms., Inc.*, 2013 WL 6865692, at *6, *12 (finding that these sets of claim terms did not require further elaboration for the fact finder to understand their meaning, and affording the terms their plain and ordinary meaning).

2. "said composition being of a quantity at least sufficient to provide multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose"

As noted above, after a discovery dispute arose, (*see* D.I. 141), the parties sought and received permission to engage in additional claim construction briefing, (D.I. 158). The briefing addressed only a single term: "said composition being of a quantity at least sufficient to provide multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose[.]" (*See* D.I. 162 at 3; D.I. 163 at 2)

The term at issue appears in Claim 5 of the '829 patent (the parties refer to it, in shorthand, as the "final term in Claim 5"). Claim 5 recites:

> A pharmaceutical composition for therapeutic use for the treatment of human beings comprising:

> [a] a pharmaceutically acceptable composition which is a (6S) diastereoisomer selected from the group consisting of (6S) leucovorin (5-formyl-(6S)-tetrahydrofolic acid) and pharmaceutically acceptable salts and esters of (6S) leucovorin, wherein the composition consists of a mixture of (6S) and (6R) diastereoisomers and consists of at least about 92% by weight of the (6S) diastereoisomer, the balance of said composition consisting of the (6R) diastereoisomer; and
>
> [b] a pharmaceutically acceptable carrier; and
>
> [c] *said composition being of a quantity at least sufficient to provide multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose.*

('829 patent, col. 10:9-24 (emphasis and [a], [b] and [c] notations added)) The claim term at issue is italicized above in the section indicated by the Court as sub-part [c]. Plaintiffs propose that this final term of Claim 5 be construed to mean "there being enough of the pharmaceutically acceptable composition to produce two or more doses of the claimed mixture of (6S) and (6R) diastereoisomers at 2000 mg per dose[.]" (D.I. 163 at 2) Defendants propose it be construed as "the 'pharmaceutically acceptable composition' contains enough of the (6S)/(6R) mixture that, once the mixture is combined with the 'pharmaceutically acceptable carrier,' the resulting 'pharmaceutical composition for therapeutic use' provides two or more doses of, at minimum, 2000 mg per dose of the mixture." (*Id.*) Although it is not clear from reading these two competing constructions, the primary dispute here appears to be whether the final term of Claim 5 recites a single composition meeting the minimum weight requirement found in sub-part [c], or whether that weight requirement may be met by aggregating multiple, separately-packaged "compositions." (*See* D.I. 170 at 5; D.I. 172 at 8) Plaintiffs believe such aggregation is proper; Defendants do not. (D.I. 172 at 6-8)

Claim 5 describes the components of a composition suitable for treating medical conditions in human beings. (*See* D.I. 85 at 2) It is a "composition" that "consists of" sub-part [a]'s "pharmaceutically acceptable composition" combined with the "pharmaceutically acceptable carrier" of sub-part [b]. ('829 patent, col. 10:9-21; D.I. 163 at 6) Sub-part [c]—the focus of the parties' proposed constructions—provides a minimum weight requirement, mandating that the "pharmaceutically acceptable composition" of sub-part [a] be of a "quantity at least sufficient to provide multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose." ('829 patent, col. 10:21-24; D.I. 163 at 4) Together, these components form Claim 5's referenced "pharmaceutical composition for therapeutic use[.]" (*See* '829 patent, col. 10:9-24) Defendants' proposed construction incorporates all of these elements, in essence construing sub-part [c] by explaining how it fits within the larger structure of Claim 5. Plaintiffs' construction alters the word order (and to a small degree, the words) of sub-part [c], but the wording used does not really flesh out Plaintiffs' position with regard to the parties' primary dispute.

While Defendants' proposed construction is at least somewhat helpful in resolving the dispute (in that it places sub-part [c] within its proper context in the claim), the true focus of Defendants' argument is quite nuanced. Defendants emphasize the word "the" in their proposed construction (i.e., "*the* 'pharmaceutically acceptable composition' contains . . .") and in the construction ultimately adopted in the Nevada Order. (D.I. 170 at 5) They argue that the use of "the" in this context mirrors how this "pharmaceutically acceptable composition" is referenced in Claim 5, since the claim recites a *single* composition, and not a collection of compositions. (*Id.*) And, indeed, this is a fair reading of the wording of Claim 5 as a whole and of the final term of

Claim 5. That is, when the claim refers to the pharmaceutically acceptable composition, it is referring to *one* composition, not many different compositions taken together or considered as a whole.

The specification and prosecution history together also provide some insight on this dispute. The specification generally highlights the importance of obtaining "good yield" in the separation of leucovorin; it contrasts this to the generation of "low" yields in the prior art. ('829 patent, col. 2:16-29) Numerous statements made in the prosecution history highlight the importance of quantity, i.e., "good yield[,]" in the kind of composition at issue in Claim 5. When faced with Claim 5's rejection, for example, the applicants' Appeal Brief to the PTO stated that "the prior art only allowed the production of leucovorin in low yields . . . [;] [h]igh yield . . . leucovorin is specifically stated to be available from the invention." (D.I. 164, ex. 9 at 13) Later in that brief, when addressing a different basis for Claim 5's rejection—its rejection as obvious over Rees 1986—the applicants noted that "*the composition*" in what is now Claim 5 includes "more stringent quantity limitations[.]" (*Id.* at 24-25 (emphasis added)) Even more telling, within this same section the applicants stated that what is now Claim 5 "require[s] a minimum of four grams" of the "mixture[,]" and for that reason, "[t]here is absolutely no basis to allege that Rees [1986] renders obvious such a *composition*." (*Id.* at 26 (emphasis added)) The applicants' emphasis on quantity and a single "composition" would make little sense if they believed that the minimum weight requirement could be met by aggregating multiple, separately-packaged "compositions." Accordingly, the prosecution history (in conjunction with the specification) provides support for Defendants' position here.

Plaintiffs fail to point to any evidence suggesting that Claim 5's minimum weight

requirement found in sub-part [c] may be met by aggregating multiple, separately-packaged or grouped-together "compositions." Instead, Plaintiffs raise two other issues: (1) that Defendants are improperly seeking construction of claim language based on the accused product, and (2) that Defendants' proposed construction improperly formulates the quantity in terms of a dosage amount that must be administered to patients. (D.I. 172 at 1-2; D.I. 162 at 9-10) The Court will address these issues in turn.

As to Plaintiffs' first argument, it is true that Defendants made numerous references to the accused product in their arguments regarding claim construction here. (*See, e.g.*, D.I. 163 at 1; D.I. 170 at 4) The Federal Circuit has stated, however, that "awareness of [the] accused [product] is permissible" in claim construction, *Aero Prods. Int'l, Inc. v. Intex Recreation Corp.*, 466 F.3d 1000, 1012 n.6 (Fed. Cir. 2006), and indeed that "knowledge of [the accused] product . . . provides meaningful context" for claim construction analysis, *Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322, 1326–27 (Fed. Cir. 2006). What is prohibited—and what the Court has not done here—is to "constru[e] claims with an aim to include or exclude an accused product[.]" *Id.* at 1326. To the extent that Defendants have referred to the accused product, those references have simply helped crystallize the nature of the actual claim construction dispute that is at issue here. And at all times, the Court's analysis here has focused solely on discerning the meaning of certain claim language as informed by the intrinsic evidence.

Plaintiffs' second point, regarding the dosage amount that must be administered to patients, has merit and ultimately affects the Court's construction of the disputed term. Plaintiffs argue that Defendants' proposed construction, which states in part that the pharmaceutical composition for therapeutic use "*provides* two or more doses [of,] at minimum, 2000 mg per

dose" of the mixture could be read to improperly "formulate[] the quantity in terms of a dosage amount that has to be administered to patients[.]" (D.I. 162 at 9 (emphasis in original))

Although Defendants proposed no alternative claim construction in their responsive brief, it appears that the parties are largely in agreement that Claim 5 is directed to, in Plaintiffs' words, "'a composition of a quantity[,]'" (*see* D.I. 162 at 9 (internal quotation marks and citation omitted)), and not the dosage amount ultimately administered to patients. (*See* D.I. 170 at 1 n.1 (Defendants acknowledging that they are "not proposing that 2000 mg . . . [is an] acutal dosage[]"); *see also id.* at 2 (Defendants arguing that Claim 5 is "directed to a composition of *a quantity able to provide* 2000 mg doses over multiple days") (emphasis added); *id.* at 5 (Defendants advocating for a construction requiring that "a *single composition be able to provide* 2000 mg doses over multiple days") (emphasis added)) Such an understanding is more consistent with the claim language, which calls for a "a *quantity at least sufficient to provide* multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose." ('829 patent, col. 10:22-24 (emphasis added)) Also, as discussed above, this focus on total quantity, rather than the administered dosage, is consistent with the specification and prosecution history of the '829 patent. As it appears that the parties agree on this point, and because it is clear that the minimum total quantity of the "mixture" that must be achieved in Claim 5 is 4000 mg (i.e., sufficient to provide "multiple doses . . . in an amount of 2000 mg per dose"), the Court will incorporate this understanding into its construction of the disputed term. (*See* D.I. 164, ex. 9 at 26 (applicants stating in their Appeal Brief to the PTO that Claim 5 "require[s] a minimum of four grams[,]" i.e., 4000 mg, of the "mixture"))

Ultimately, the Court agrees with Defendants that the final term of Claim 5 refers to one

single composition meeting the minimum weight requirement found in sub-part [c], as is demonstrated through the claim's language, the specification and its prosecution history. In light of this and the Court's recognition that total quantity, not administered dosage, is the focus of this Claim, the Court construes the final term of Claim 5 to mean "the 'pharmaceutically acceptable composition' contains enough of the (6S)/(6R) mixture that, once the mixture is combined with the 'pharmaceutically acceptable carrier,' the resulting 'pharmaceutical composition for therapeutic use' contains, at minimum, 4000 mg of the mixture."

C. Conclusion

For the foregoing reasons, the Court recommends that the District Court adopt the following constructions:

1. "the balance of said compound consisting of the (6R) diastereoisomer" means "the remaining amount of the mixture of (6S) and (6R) diastereomers is the (6R) diastereoisomer, and any impurities normally associated with the mixture of (6S) and (6R) diastereomers."
2. "the balance of said composition consisting of the (6R) diastereoisomer" means "the remaining amount of the mixture of (6S) and (6R) diastereomers is the (6R) diastereoisomer, and any impurities normally associated with the mixture of (6S) and (6R) diastereomers."
3. "A pharmaceutical composition for therapeutic use" means "a composition suitable for treating medical conditions."
4. "A pharmaceutical composition for therapeutic use for the treatment of human beings" means "a composition suitable for treating medical conditions in human

beings."

5. "for therapeutic use for the treatment of human beings" means "suitable for treating medical conditions in human beings."

6. "a pharmaceutically acceptable compound" means "a compound suitable for treating medical conditions which is not harmful to the recipient thereof."

7. "a pharmaceutically acceptable composition" means "a composition suitable for treating medical conditions which is not harmful to the recipient thereof."

8. "a polar solvent" means "a solvent with a dielectric constant of 15 or higher."

9. "said mixture of (6S) and (6R) diastereoisomers is present in said composition in an amount of at least about 10 grams" means "the pharmaceutical composition contains at least about 10 grams of the mixture of (6S) and (6R) diastereoisomers of leucovorin."

10. the "mixture" and "percentage" claim terms should be afforded their plain and ordinary meaning.

11. "said composition being of a quantity at least sufficient to provide multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose" means "the 'pharmaceutically acceptable composition' contains enough of the (6S)/(6R) mixture that, once the mixture is combined with the 'pharmaceutically acceptable carrier,' the resulting 'pharmaceutical composition for therapeutic use' contains, at minimum, 4000 mg of the mixture."

IV. CONCLUSION

The Court recommends that the District Court adopt the constructions set out in Section

III.C above, for the reasons discussed in Section III.A and Section III.B above.

This Report and Recommendation is filed pursuant to 28 U.S.C. § 636(b)(1)(B), Fed. R. Civ. P. 72(b)(1), and D. Del. LR 72.1. The parties may serve and file specific written objections within fourteen (14) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b)(2). The failure of a party to object to legal conclusions may result in the loss of the right to *de novo* review in the district court. *See Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1 (3d Cir. 2006); *Henderson v. Carlson*, 812 F.2d 874, 878–79 (3d Cir. 1987).

The parties are directed to the Court's Standing Order for Objections Filed Under Fed. R. Civ. P. 72, dated October 9, 2013, a copy of which is available on the District Court's website, located at http://www.ded.uscourts.gov.

Dated: July 3, 2014

Christopher J. Burke
UNITED STATES MAGISTRATE JUDGE