UNITED STATES DISTRICT COURT

DISTRICT OF NEVADA

SPECTRUM PHARMACEUTICALS, INC. and UNIVERSITY OF STRATHCLYDE, Plaintiffs, vs. SANDOZ INC., Defendant.	Case No.: 2:12-cv-00111-GMN-NJK **CORRECTED ORDER**

This Order corrects a clerical error in the original Order filed on December 31, 2013 at ECF No. 199, as follows: on page 8, FN1, diastereoisomer is corrected to read diastereoisbmer. All other aspects of the original Order remain the same.

Pending before the Court are the proposed claim constructions submitted by Plaintiffs Spectrum Pharmaceuticals, Inc. and University of Strathclyde (collectively, "Plaintiffs") and Defendant Sandoz Inc. ("Defendant"). Plaintiff filed its Opening Brief on August 27, 2012 (ECF No. 49), Defendant filed a Responsive Brief on September 10, 2012 (ECF No. 53), and Plaintiff filed a Reply Brief on September 17, 2012 (ECF No. 56). Subsequently, the Court permitted the parties to file supplemental claim construction briefing. (ECF No. 66.) Thereafter, Defendant filed its supplemental briefing on November 26, 2012 (ECF No. 75) and Plaintiffs filed their supplemental brief on December 3, 2012 (ECF No. 81). The Court held a Tutorial Hearing on December 5, 2012, and a Markman Claim Construction Hearing on December 11, 2012.

This is an Order construing the disputed terms of the claims in United States Patent No. 6,500,829 ("the '829 Patent"). The parties have submitted nine terms, phrases or groups thereof for construction. (See generally Pls.' Br. 6–30, ECF No. 49; Def.'s Resp. 5–27, ECF No. 53.) In

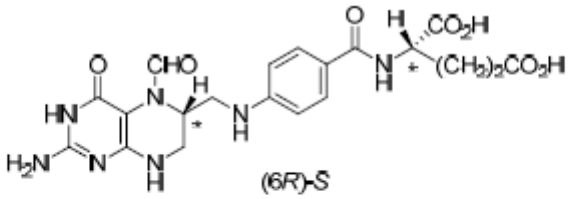
addition, the parties agree on the construction of one additional term. (See Resp. 27 n.15.) The Court will adopt the proposed claim construction for the one term on which the parties agree, as reflected herein.

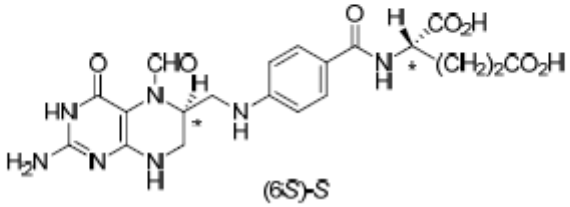
After consideration of the briefs and material submitted by the parties, the arguments of counsel at the claim construction hearing, and the record before the Court, the Court issues this Order construing the disputed claim terms.

I. BACKGROUND

5-formyl-(6R,S)-tetrahydrofolic acid is the chemical name for a compound more commonly known as leucovorin. This compound has been used since the 1950s to prevent the toxic side-effects of methotrexate, a commonly used chemotherapy agent. U.S. Patent No. 6,500,829 col.1 ll.22–24 (filed Apr. 18, 1995). Essentially, leucovorin protects the patient's healthy cells while still allowing the methotrexate to kill the cancerous cells. Id. at col.1 ll.24–29. Without leucovorin, methotrexate would also kill many of the patient's healthy cells. Id. This use of leucovorin is known as "methotrexate rescue." Id. at col.1 ll.24–29.

As the name suggests, 5-formyl-(6R,S)-tetrahydrofolic acid contains an asymmetric, or chiral, center at the 6 carbon. Id. at col.1 ll.34–35.





This chiral center causes leucovorin to exist as a 50-50 mixture of two diastereoisomers denoted as the "6R" isomer and the "6S" isomer. Id. However, only the 6S isomer, known as "levoleucovorin," is the effective methotrexate rescue agent. Id. at col.1 ll.57–61. For this

reason, scientists began attempting to separate the 6S isomer from the 6R isomer to enable administration of a higher dosage of the effective 6S isomer. Although other scientists have previously discovered methods of synthesis or isolation, these methods either produced low yields or failed to achieve reasonable purity. See id. at col.2 ll.13–23.

In response to the shortcomings of the prior art methods of separating and purifying levoleucovorin, a team of researchers from Plaintiff University of Strathclyde filed a patent application, which eventually issued as the '829 Patent. Specifically, the '829 Patent discloses "substantially pure" levoleucovorin compositions, which have "most preferably greater than 95%" of the (6S) isomer. Id. at col.4 ll.26–29. The '829 Patent describes that substantially pure 6R and 6S samples can be achieved in good yield by introducing a "chiral auxiliary group into tetrahydrofolate or a tetrahydrofolate derivative" close to the chiral center at the 6 carbon. Id. col.2, ll.24-29. The '829 Patent further discloses that "[t]he pair of new diastereoisomers so created [could] be separated by standard techniques such as crystallisation, chromatography, solvent extraction and similar methods." Id. col.3 ll.42–45. The chosen method of purification can be repeated to improve purity. Id. col.3 ll.54–56. "Conveniently the step may be repeated until the recovered new diastereoisomer has a purity greater than 90%." Id. col.3 ll.56–58.

After filing a New Drug Application ("NDA") with the FDA, Plaintiff Spectrum Pharmaceuticals, Inc. received approval to market this substantially pure form of levoleucovorin under the trade name "Fusilev®." The FDA approved Fusilev® "to treat patients diagnosed with advanced metastatic colorectal cancer . . . to effect 'methotrexate rescue.'" (Pls.' Claim Construction Br. 4:2–4, ECF No. 49.)

In 2011, Defendant Sandoz filed an Abbreviated New Drug Application ("ANDA") with the FDA, pursuant to 21 U.S.C. § 355(j), seeking to market a proposed generic version of Fusilev®. As required by section 355(j)(2)(A)(vii), Defendant certified in its ANDA that the manufacture, use, or sale of its generic version of Fusilev® would not infringe any valid,

enforceable claim of any patent that covers Fusilev®. In addition, as required by section 355(j)(2)(B)(iii), Defendant provided notice of its ANDA to the owner of the '829 Patent, Plaintiff University of Strathclyde, 21 U.S.C. § 355(j)(2)(B)(iii)(I), and to the holder of the approved NDA that is covered by the '829 Patent, Plaintiff Spectrum Pharmaceuticals, 21 U.S.C. § 355(j)(2)(B)(iii)(II).

In response, Plaintiffs filed the instant action alleging infringement of the '829 Patent. (Compl. ¶¶ 21–28, ECF No. 1.) Specifically, Plaintiffs assert that Defendant's proposed generic levoleucovorin product infringes claims 1, 2, and 5–14 of the '829 Patent. (Pls.' Claim Construction Br. 4:14.)

II. LEGAL STANDARD

The resolution of patent infringement actions generally requires two distinct steps. First, the Court engages in a claim construction analysis to "determin[e] the meaning and scope of the patent claims asserted to be infringed." Markman v. Westview Instruments, Inc., 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), aff'd 517 U.S. 370 (1996). Only once the claims are properly construed does the action proceed to the second step, in which the factfinder compares those properly construed claims to the accused device to determine, as a matter of fact, whether all of the claim limitations are present in the accused device. Id. At the current stage of this patent infringement action, the Court focuses only on the first step.

A. Claim Construction

"It 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." Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed.Cir.2005) (en banc) (citations and internal quotation marks omitted). The interpretation of the scope and meaning of disputed terms in patent claims is a question of law and exclusively within the province of a court to decide. Markman, 517 U.S. at 372. When construing disputed claim terms, the Court must give each disputed term "the meaning that the term would have to a

person of ordinary skill in the art at the time of the invention," unless the patentee clearly intended a different definition. Phillips, 415 F.3d at 1312–13. Furthermore, "the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears but in the context of the entire patent, including the specification." Id. at 1313.

In certain cases, "the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." Id. at 1314. In other instances, the claim term may have a particular meaning in the field of art that is not immediately clear. Id. In such cases, the Federal Circuit has instructed that a court's analysis should focus on the intrinsic evidence, including "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." Id. at 1314. "[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms." Id. "Other claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment as to the meaning of a claim term." Id. Specifically, differences between the claims often provide useful guidance in understanding the meaning of the claim terms. Id. "For example, 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.

The claims, however, are not read in isolation, but are read in light of the entire specification, of which the claims are a part. Id. In fact, the specification is "the single best guide to the meaning of a disputed term." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996). Courts can also look to the prosecution history as part of the intrinsic record to determine how the Patent Office and the inventor understood the patent. Phillips, 415

F.3d at 1317. However, the prosecution history lacks the clarity of the specification and more often is less useful for claim construction purposes. Id.

Finally, extrinsic evidence may also be relevant to claim construction. Id. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Markman, 52 F.3d at 980. Although such evidence may aid the Court in construing claim terms, "it is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." Phillips, 415 F.3d at 1319. Thus, "while extrinsic evidence can shed useful light on the relevant art, . . . it is less significant than the intrinsic record in determining the legally operative meaning of claim language." Id. at 1317 (internal quotation marks omitted).

III. THE LEVEL OF ORDINARY SKILL

Patent claims are to be construed to reflect the understanding of an ordinary worker in the appropriate field. Phillips, 415 F.3d at 1312–13 ("[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention . . .."). Thus, in the claim construction process, the Court first determines the level of ordinary skill in the relevant technology. In making this determination, the Court considers the complexity of the technology, the pace of technological advancement in the field, and the education and experience of those working in the area. See Daiichi Sankyo Co., Ltd. v. Apotex, Inc., 501 F.3d 1254, 1257 (Fed. Cir. 2007).

In this case, both parties agree that the appropriate level of skill is "a Ph.D. in organic chemistry with some industrial, or post-doctoral experience." (Jones Decl. ¶ 8, ECF No. 55; see also Pls.' Br. 8, n.31, ECF No. 49 (stating that, in the context of the '829 Patent, "one of ordinary skill in the art" would typically be a "Ph.D. chemist[] with some industrial experience").)

/ / /

IV. CONSTRUCTION OF THOSE TERMS ON WHICH THE PARTIES AGREE

In Defendant's Responsive Claim Construction Brief, Defendant stated its agreement with Plaintiffs' proposed construction of "said composition is produced as a result of separation by differential solubility" (Def.'s Resp. Claim Construction Br. 27 n.15, ECF No. 53 ("Upon review of Plaintiffs' brief and their statements regarding the claim term 'said composition is provided as a result of separation by differential solubility . . . ,' Sandoz now agrees with Plaintiffs' proposed construction of that term.").) The Court hereby adopts this proposed construction. Therefore, the Court construes the term "said composition is produced as a result of separation by differential solubility" as "the pharmaceutically acceptable composition is produced as a result of separation by differential solubility in a polar solvent of a (6S) diastereoisomer from an initial mixture containing equal amounts of (6S) and (6R) diastereoisomers." (Pls.' Br. 29:11–18.)

V. CONSTRUCTION OF THE DISPUTED CLAIM TERMS

In their respective claim construction briefs, the parties identified nine categories of claim terms that are in need of the Court's construction: (1) "mixture"; (2) the "percentage" claim terms; (3) "the balance of said compound consisting of the (6R) diastereoisomers"; (4) "pharmaceutical composition for therapeutic use (for the treatment of human beings)"; (5) "pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings"; (6) the "pharmaceutically acceptable" claim terms; (7) "consists essentially of"; (8) the "multiple dose" claim terms; and (9) claim 13's reference to claim 11 and claim 14's reference to claim 10. The disputed claim terms are emphasized below.

Claim 1:

> 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) diastereoisomers 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.

Claim 5:

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

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

a pharmaceutically acceptable carrier; and

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**.

Claim 10:

A **pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings** consisting of a **mixture** of:

a (6S) diastereois[o]mer[1] 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;

wherein said **mixture** of (6S) and (6R) diastereoisomers consists of **at least about 92% by weight** of the (6S) diastereoisomer, **the balance of said composition consisting of the (6R) diastereoisomer**; and

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

Finally, the parties dispute whether claims 13 and 14 are drafted in dependent or independent form and also dispute the validity of these two claims.

---

[1] The originally issued claim 10 recited "a (6S) diastereoisbmer . . .." '829 Patent col.10 l.50. However, the '829 Patent includes a Certificate of Correction, dated May 6, 2003, which provides that claim 10 should recite "a (6S) diastereoisomer . . .."

A. "Mixture"

Proposed Constructions[2]

Spectrum	Plain Meaning: "a mixture of (6S) and (6R) diastereoisomers of leucovorin"
Sandoz	"a two-component combination consisting of non-negligible amounts of each of the (6S) and (6R) diastereoisomers, and excludes pure (6S) diastereoisomers"

The term "mixture" appears in Claims 1, 5-7, and 10-12.

1. Plaintiffs' Proposed Construction

Plaintiffs contend that the term "mixture" needs no further construction. (See Pls.' Br. 11:17–12:8, ECF No. 49.) Essentially, Plaintiffs argue that the term "mixture" is clear on its face and, as a result, no further understanding or explanation is needed.

"The construction of claims is simply a way of elaborating the normally terse claim language in order to understand and explain, but not to change, the scope of the claims." Terlep v. Brinkmann Corp., 418 F.3d 1379, 1382 (Fed. Cir. 2005) (citations omitted). Furthermore, when the claim language is "clear on its face," then the Court's "consideration of the rest of the intrinsic evidence is restricted to determining if a deviation from the clear language of the claims is specified." Interactive Gift Exp., Inc. v. Compuserve Inc., 256 F.3d 1323, 1331 (Fed. Cir. 2001).

Here, the term "mixture" needs no further construction; this is not the type of "terse claim language" that needs further elaboration before the jury will understand the meaning of the phrase. The Court finds that one of skill in the art would need no further explanation, other than the words of the claim, to determine the identity of the components in the claimed "mixture." For the same reason, the Court concludes that one of skill in the art would understand that a "mixture" requires the presence of both of the components listed in the claim language. There is

---

[2] Throughout this Order, Plaintiffs' proposed constructions are taken from their Opening Claim Construction Brief. (See ECF No. 49.) Similarly, throughout this Order, Defendant's proposed constructions are taken from its Responsive Claim Construction Brief. (See ECF No. 53.)

no evidence in the words of the ’829 Patent that indicate that the term “mixture” is used in anything other than its ordinary meaning. See O*2 Micro Int’l Ltd. v. Beyond Innovation Tech.* Co., Ltd., 521 F.3d 1351, 1361 (Fed. Cir. 2008) (“A determination that a claim term ‘needs no construction’ or has the ‘plain and ordinary meaning’ may be inadequate when a term has more than one ‘ordinary’ meaning or when reliance on a term’s ‘ordinary’ meaning does not resolve the parties’ dispute”).

2. *Defendant’s Proposed Construction.*

Defendant requests that this Court construe the term “mixture” as “a two-component combination consisting of non-negligible amounts of each of the (6S) and (6R) diastereoisomers, and excludes pure (6S) diastereoisomers.” For the reasons discussed below, the Court disagrees that such construction is correct.

a. *“non-negligible”*

Defendant first argues that its construction is correct because, without the “non-negligible” language, the “(6R) diastereoisomers” and “mixture” limitations would be rendered meaningless. (Resp. 5:18–21, ECF No. 53.) However, the Court is not persuaded that Defendant’s proposed construction must be adopted to limit the ’829 Patent to “substantially pure” diastereoisomers rather than “pure” diastereoisomers.

First, the claim language itself expressly recites a composition that contains both isomers. ’829 Patent col.9, ll.62–64. Furthermore, the specification states that the ’829 Patent relates to the preparation of “substantially pure diastereoisomers.” Accordingly, the Court agrees with Defendant that one of skill in the art would not read the ’829 Patent as claiming “pure” (6S) diastereoisomers. Nevertheless, the Court is not persuaded that this alone requires that the construction of “mixture” include the term “non-negligible.” In fact, the Court is concerned that incorporating “non-negligible” would create additional confusion and require subsequent determination of how much (6R) isomer need be present to indeed be “non-negligible.”

Additionally, contrary to Defendant's assertions, the omission of "non-negligible" from the construction of "mixture" does not expand the claim scope to cover "pure" (6S) isomer because a mixture of the two isomers cannot exist if one of the isomers is completely absent. The very term "mixture" requires that each isomer be present in the composition in some detectable amount.

Having provided no additional basis for the inclusion of the "non-negligible" language in the construction of "mixture," the Court finds that Defendant has failed to provide language from the specification of the '829 Patent that would require such a limitation. Therefore, the Court declines to adopt this portion of Defendant's proposed construction.

b. *"two*-component c*ombination"*

Defendant also argues that the Court should limit the claimed "mixture" to a "two-component combination" because "in a patent claim, the transitional phrase 'consists of' signifies the exclusion of any ingredient not specified in the claim and the asserted claims describe two components, (6S) and (6R) leucovorin." (Resp. 6:18–21 (citing In re Crish, 393 F.3d 1253, 1257 (Fed. Cir. 2004).) Plaintiffs, on the other hand, argue that neither the claim language nor the words of the remainder of the specification support Defendant's construction. (Pls.' Br. 13:20–24.)

In Crish, the Federal Circuit examined three claims that contained the phrase "consists of" within the body of the claim. 393 F.3d at 1254–55:

> Claims 53-55 on appeal are all independent and read as follows:
>
> 53. A purified oligonucleotide comprising at least a portion of the nucleotide sequence of SEQ ID NO:1, **wherein said portion consists of the nucleotide sequence from 521 to 2473 of SEQ ID NO:1**, and wherein said portion of the nucleotide sequence of SEQ ID NO:1 has promoter activity.
>
> 54. A purified oligonucleotide comprising at least a portion of the nucleotide sequence of SEQ ID NO:1, **wherein said portion consists of the nucleotide sequence from 1141 to 2473 of SEQ ID NO:1**, and wherein said portion of the nucleotide sequence of SEQ ID NO:1 has promoter activity.

> 55. A purified oligonucleotide comprising at least a portion of the nucleotide sequence of SEQ ID NO:1, **wherein said portion consists of the nucleotide sequence from 1488 to 2473 of SEQ ID NO:1**, and wherein said portion of the nucleotide sequence of SEQ ID NO:1 has promoter activity.

Id. (emphasis added). Based on this claim language, the Federal Circuit held that "the term 'consists' limits the 'said portion' language to the subsequently recited nucleotides." Furthermore, in the relevant claim language, the "said portion" language was located before the "consists of" language that acted to limit "said portion" to the subsequently stated nucleotide sequence. Id. at 1254–55.

In the instant case, the claim language of the '829 Patent is distinguishable and, thus, does not warrant the same conclusion that the Federal Circuit reached in Crish. Contrary to Defendant's assertion that the term "consists of" limits the term "a mixture," the term "consists of" appears after the term "the compound." '829 Patent col.9 ll.62–64. Thus, "consists of" actually limits "the compound," and not "the mixture." Id. Accordingly, the Court is not persuaded that Crish requires the term "mixture" to be limited to a "two-component combination."

Having provided no additional basis for the inclusion of the "two-component combination" language in the construction of "mixture," the Court finds that Defendant has failed to provide the Court with language from the specification of the '829 Patent that would require such a limitation. Therefore, the Court declines to adopt this portion of Defendant's proposed construction.

3. *The Court's Construction*

After looking first to the words of the claim and then the remaining parts of the specification, the Court finds that a person of ordinary skill in the art of organic chemistry would understand the '829 Patent to use the term "mixture" in accordance with that phrase's plain meaning. This phrase needs no further construction.

B. The "Percentage" Claim Terms

Proposed Constructions

"consists of (at least 92%)(at least about 92%)(at least about 95%) by weight of the (6S) diastereoisomers"	**Spectrum**	"contains (92% or more)(about 92% or more)(greater than 95%) by weight of the (6S) diastereomer"
	Sandoz	"the [compound] consists of (6S) diastereoisomers with diastereomeric purity of (at least 92%)(at least about 92%)(greater than 95%) by weight and up to 98% by weight"
"said mixture of (6S) and (6R) diastereoisomers consist of (at least about 92%)(at least about 95%) by weight of the (6S) diastereoisomers"	**Spectrum**	"the mixture of (6S) and (6R) diastereoisomers of leucovorin contains (about 92% or more)(about 95% or more) by weight of the (6S) diastereoisomers"
	Sandoz	"the two-component combination consisting of non-negligible amounts of (6R) diastereoisomers and (6S) diastereoisomers with diastereomeric purity (at least about 92%)(at least about 95%) by weight and up to 98% by weight"

Some form of these "percentage" claim terms appears in Claims 1, 2, 5, 7, 10, and 12.

1. *Defendant's Proposed Construction*

Defendant's proposed construction amounts to an upper limit on the purity of the compound claimed in the '829 Patent. Defendant asserts that its proposed construction "define[s] [an] upper limit, and do[es] so by reference to the specification and the prosecution history, including the inventor's own declarations, and arguments the applicants made in order to obtain allowance of the '829 patent." (Resp. 14:22–24, ECF No. 53.)

Specifically, Defendant argues that the '829 Patent should be limited to a compound containing at most 98% by weight (6S) diastereoisomer. Defendant supports its proposed construction with Example 1 in the written description, which describes a butanol extraction that yields a mixture with 91% and 92% purity of the (6S) diastereoisomer. '829 Patent col.6, l.51–col.7 l.10. Defendant further asserts that repeated rounds of butanol extractions would not lead

to any significant increase in purity and, thus, an upper limit must be imposed on the percentage claim terms. Defendant further argues that such an upper limit is warranted because the separation method described in the specification of the '829 Patent could not achieve greater than a 98% pure (6S) diastereoisomer composition.

These arguments are unavailing. First, the Court finds no support for Defendant's proposed construction in the intrinsic evidence. In fact, Phillips instructs that a court should look to the words of the claims themselves when construing claim terms and, here, the words of the other claims in the '829 Patent contradict Defendant's proposed construction. Specifically, claim 4 expressly includes an upper limitation on the diastereomeric purity of the composition. '829 Patent, col.10 ll.7–9 (claiming a "pharmaceutical composition . . . which consists essentially of 92% to 95% by weight of the (6S) diastereoisomers"). The existence of an upper limit in one claim indicates that, if the patentee had intended to impose an upper limitation in the other claims, such an upper limit would also be stated explicitly in those other claims.

Additionally, adopting Defendant's proposed construction, which largely relies on Example 1, would result in the Court impermissibly limiting the '829 Patent to a preferred embodiment. Phillips, 415 F.3d at 1323 ("[W]e have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment.").

Additionally, Defendant argues that its construction is consistent with the prosecution history of the '829 Patent. However, Defendant's arguments in support of its proposed construction are actually related to the defenses of lack of enablement and/or inadequate written description and are thus, improper at the claim construction stage of the litigation. Specifically, during prosecution, the USPTO rejected certain claims of the '829 Patent because the specification failed to enable compositions that were greater than 95% (6S) diastereoisomer. To overcome this lack of enablement rejection, one of the inventors, Dr. Suckling, submitted a

sworn declaration stating that "the purity . . . taking into account the intrinsic error is in the range of about 90-98%." (Keane Decl. Ex. 7, ECF No. 60; Jones Decl. ¶ 64, ECF No. 61.) However, this statement alone is insufficient to amount to a disavowal of claim scope beyond 98% purity. Indeed, the Federal Circuit routinely "decline[s] to apply the doctrine of prosecution disclaimer where the alleged disavowal of claim scope is ambiguous." Omega *Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1324 (Fed. Cir. 2003) (reciting cases in which the Federal Circuit has found the asserted disavowal too ambiguous to limit the scope of the claims). In contrast, Dr. Suckling's declaration was provided to the PTO merely to establish that the specification adequately enabled the claims that recite purities above 95% (6S) diastereoisomer. Accordingly, the Court finds that Defendant has failed to cite language in the file wrapper amounting to an unambiguous statement disavowing all pharmaceutical compositions with greater than 98% purity.

Defendant's final argument relates to USPTO's rejection in light of the prior art reference, Rees 1986. In overcoming that rejection, the inventors distinguished their invention to the USPTO as making "mixtures of (6S) and (6R) diastereoisomers," and not pure (6S) diastereoisomer as described in the Rees 1986 reference. (Keane Decl. Ex. 2, at 23, ECF No. 54-2.) Defendant further asserts that "[a] person having ordinary skill in the art would understand that the Rees 1986 product that the applicants disclaimed and described as "pure (6S) diastereoisomer" in fact contained about 98% by weight (6S) diastereoisomer and 2% by weight (6R) diastereoisomer." (Jones Decl. ¶¶ 37–59, ECF No. 61.)

This argument is also unpersuasive because it is based on the extrinsic re-interpretation by Defendant's retained expert, Dr. Jones, of the underlying data supporting the Rees 1986 reference, rather than the words of the reference and how one of skill in the art would understand those words. See Phillips v. AWH Corp., 415 F.3d 1303, 1318 (Fed. Cir. 2005) (en banc) ("[A] court should discount any expert testimony 'that is clearly at odds with the claim

construction mandated by the claims themselves, the written description, and the prosecution history, in other words, with the written record of the patent." (internal quotations marks omitted)). In fact, Dr. Jones, expressly admits that one of skill in the art would read the Rees 1986 reference as disclosing a product that is solely the (6S) diastereoisomer without the presence of the (6R) diastereoisomer. (Antons Decl. Ex. 1 (Jones Dep. Tr.), at 6:11-23, ECF No. 82-1 (acknowledging that the authors of the Rees 1986 reference actually indicated that they achieved a single product and that one of ordinary skill in the art would also understand that the Rees 1986 reference disclosed a single product).) Nevertheless, Defendant's retained expert concludes that the Reese 1986 reference was incorrect when it concluded that the resulting substance was a pure (6S) diastereoisomer product. However, Defendant and its retained expert do not argue that one of skill in the art would read the words of the Rees 1986 reference as disclosing a compound that contains 2% (6R) diastereoisomer. Rather, Defendant merely argues that its expert disagrees with the conclusions made by the authors of the Rees 1986 reference. Essentially, Defendant's argument amounts to "second-guessing" the conclusions in the Rees 1986 reference and, thus, does not persuade the Court to adopt Defendant's proposed construction.

Even to the extent that there is a minor reference in a footnote of the Rees 1986 to a compound containing small amounts of the (6R) diastereoisomer, [3] this reference does not rise to the level of the unambiguous statement of disavowal required to establish a prosecution

---

[3] Defendant points out that, in a footnote, the Rees 1986 reference cited a 1983 article by Rees and a 1985 article by Suckling. Defendant correctly notes that "[m]aterial not explicitly contained in [the prior art reference] may still be considered . . . if that material is incorporated by reference into the document." Advanced Display Sys., Inc. v. Kent State Univ., 212 F.3d 1272, 1282 (Fed. Cir. 2000). However, merely citing an article in a footnote does not result in that entire article being incorporated by reference to the later published article; before such an article can be incorporated by reference, the later article "must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents." Id.; see also Commonwealth Scientific & Indus. Research Org. v. Buffalo Tech. (USA), Inc., 542 F.3d 1363, 1372 (Fed. Cir. 2008) (concluding that content from a reference that is merely cited in a footnote is not incorporated by reference into the prior art reference because the prior art failed to "identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents").

disclaimer. See Abbott Labs. v. Sandoz, Inc., 566 F.3d 1282, 1289 (Fed. Cir. 2009) ("Again owing in part to the inherent ambiguities of prosecution history, the doctrine of prosecution disclaimer only applies to unambiguous disavowals."). As before, Defendant's argument is more appropriately raised in support of one of the various defenses to patent infringement.

Finally, the Federal Circuit has confronted similar language in the past and acknowledged that "at least" limitations "set[] forth the minimum number of a particular element required." Lantech Inc. v. Keip Mach. Co., 32 F.3d 542, 546 (Fed. Cir. 1994) (construing the term "at least two" to "require two or more conveyor structures, not one"). Similarly, in Quantum Corp. v. Rodime, PLC, the Federal Circuit expressly recognized that "'at least 600 tpi' . . . expressly represents an open-ended range"). 65 F.3d 1577, 1581 (Fed. Cir. 1995). Thus, although the requirement that this composition exist as a "mixture" of the two diastereoisomers eliminates the possibility of the '829 Patent covering a completely pure form of (6S) levoleucovorin, there is no indication that the patent requires as much as 2% by weight of the undesirable (6R) diastereoisomer.

2. Plaintiffs' Proposed Construction

Plaintiffs contend that these "percentage" claim terms need no further construction. (See Pls.' Br. 6:16–17.) Essentially, Plaintiffs argue that these terms are clear on their face and, as a result, no further understanding or explanation is needed. In response to Defendant's Proposed Construction, Plaintiffs assert that the imposition of an upper limit on the purity of the mixture finds no support in the specification and, in fact, contradicts the language of the written description. Specifically, Plaintiffs note that the '829 patent "teaches that when a very high percentage of the (6S) isomer is desired, the crystallization (shown above as a 'butanol extraction') can be repeated over and over until the desired percentage is obtained: 'Where appropriate more than one solvent extraction or fractional crystallisation step may be carried out in order to improve purity.'" (Pls.'Br. 8:5–9, ECF No. 49 (citing '829 Patent col.3 ll.54–56).)

The patent further teaches that "the [solvent extraction or fractional crystallisation] step may be repeated until the recovered new diastereoisomers has a purity greater than 90%." '829 Patent col.3, ll.56–58. Plaintiff asserts that, from this, one of skill in the art would know that "subsequent rounds of separation would improve the 91%-pure mixture to 99%-pure mixture or higher." (Pls.' Br. 8:13–15, ECF No. 49 (citing Reider Decl. ¶ 25, ECF No. 51).)

The Court agrees with Plaintiffs that the upper limit that Defendant would impose in this claim language is supported by neither the intrinsic evidence nor the Federal Circuit's precedent. See Lantech Inc. v. Keip Mach. Co., 32 F.3d 542, 546 (Fed. Cir. 1994) (construing the term "at least two" to "require two or more conveyor structures, not one"). The Court also agrees that this is not the type of "terse claim language" that needs elaboration to allow the factfinder to understand the scope of the claims. See Terlep v. Brinkmann Corp., 418 F.3d 1379, 1382 (Fed. Cir. 2005).

3. *The Court's Construction*

After looking first to the words of the claim and then the remaining parts of the specification, the Court finds that a person of ordinary skill in the art of organic chemistry would understand the '829 Patent to use these "percentage" claim terms in accordance with their plain meaning. These phrases need no further construction.

C. "the balance of said composition consisting of the (6R) diastereoisomer"

Spectrum	"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"
Sandoz	"the balance of (the compound) (the composition) consists of a non-negligible amount of the (6R) diastereoisomer"

This phrase appears in claims 1, 5, 7, 10 and 12.

1. *The Parties' Proposed Constructions*

In the claims of the '829 Patent, this phrase follows the previously discussed "mixture" and "percentage" claim terms and recites that the portion of the mixture that does not consist of

the desired (6S) diastereoisomer, consists of (6R) diastereoisomer. Along with many other disputed claim terms in the '829 Patent, this claim term also requires that both the (6S) and (6R) diastereoisomer are present in the claimed "pharmaceutical composition"; the '829 Patent does not cover a composition that consists solely of the (6S) diastereoisomer. Plaintiffs' proposed construction is consistent with this plain meaning.

Plaintiffs also assert that the balance of the composition that is not (6S) diastereoisomer may also consist of "any impurities normally associated with the mixture of (6S) and (6R) diastereomers." After reviewing Defendant's Responsive Claim Construction Brief, it appears to the Court that Defendant does not dispute this portion of Plaintiff's proposed construction. (See Resp. 6:18–7:6, ECF No. 53.) Indeed, both parties cite to Conoco, Inc. v. Energy & Envtl. *Int'l*, in which the Federal Circuit held that the transitional phrase "consisting of," closes the claim "to the inclusion of materials other than those recited except for impurities ordinarily associated therewith." 460 F.3d 1349, 1360 (Fed. Cir. 2006) ("[I]mpurities that a person of ordinary skill in the relevant art would ordinarily associate with a component on the 'consisting of' list do not exclude the accused product or process from infringement.") In its brief, Defendant explains that, because its proposed construction retained the "consists of" language, this additional language in the construction was unnecessary. However, given that the Federal Circuit has already endorsed this definition, the Court will adopt this portion of Plaintiffs' proposed construction to provide further guidance to the factfinder.

Finally, in Defendant's proposed construction, Defendant, once again, inserts "non-negligible" into the construction. For the reasons previously stated in Section V.A.2.a, the Court declines to adopt Defendant's "non-negligible" construction.

2. *The Court's Construction*

After looking first to the words of the claim and then the remaining parts of the specification, the Court finds that a person of ordinary skill in the art of organic chemistry would

understand the'829 Patent to use the phrase "the balance of said compound consisting of the (6R) diastereoisomer" as meaning "the remaining amount of the mixture of (6S) and (6R) diastereoisomers is the (6R) diastereoisomer, and any impurities normally associated with the mixture of (6S) and (6R) diastereoisomers."

D. "Pharmaceutical composition for therapeutic use"

Spectrum	"[A] pharmaceutical composition suitable for treating medical conditions"
Sandoz	"[A] pharmaceutical composition in a final dosage form"

The preamble of both claim 1 and claim 5 recite "[a] pharmaceutical composition for therapeutic use." The words of a claim's preamble do not always equate to claim limitations. See Am. Med. Sys., Inc. v. Biolitec, Inc., 618 F.3d 1354, 1359 (Fed. Cir. 2010) (concluding that the preamble language "d[id] not constitute a limitation of the claims"); see also Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305 (Fed. Cir. 1999) (noting that the preamble is "of no significance to claim construction [when] it cannot be said to constitute or explain a claim limitation"). "In general, a preamble limits the invention if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim." *Catalina Mktg. Int'l, Inc. v.* Coolsavings.com, Inc., 289 F.3d 801, 808 (Fed. Cir. 2002) (quoting Pitney Bowes, 182 F.3d at 1305). Here, the parties agree that the preamble language, "a pharmaceutical composition for therapeutic use," imposes a limitation on claims 1, 5, and the claims that depend therefrom. (Pls.' Br. 18, n.64, ECF No. 49.)

1. *Defendant's Proposed Const*ruction

Defendant proposes that the Court construe the phrase "pharmaceutical composition for therapeutic use" as "a composition in a final dosage form." (Resp. 15:1–8, ECF No. 53.) Defendant contends that this construction is consistent with the claim language, the words of the other claims and the words of the written description. (Id. at 15:18–17:18.) In contrast,

Plaintiffs argue that Defendant's proposed construction is actually inconsistent with the specification, violates the doctrine of claim differentiation, and excludes a preferred embodiment. (Reply 14:12–15:19, ECF No. 56.)

Defendant first supports its proposed construction by relying on the words of independent claims 1 and 5 and the differences between those claims and independent claim 10. Both claims 1 and 5 recite a pharmaceutical composition that is used "in combination with a pharmaceutically acceptable carrier." In contrast, claim 10 omits any reference to a carrier and, instead, appears to be related to a bulk drug product that can later be used to prepare a medication that can be combined with a carrier. See '829 Patent col.10 ll.47–62 (Claim 10) (claiming "[a] pharmaceutical composition for preparing medicaments for therapeutic use . . .."). Based on these differences, Defendant asserts that the pharmaceutical composition claimed in Claims 1 through 9 must claim a pharmaceutical product in "a final dosage form" that is "formulated for administration to patients." (Resp. 15:1–12.)

Furthermore, the Court need not include the "final dosage form language" in this construction to differentiate claims 1 through 9 from claims 10 through 14; the existing words of these claims are sufficient. Specifically, claims 1, 5 and the claims that depend therefrom expressly recite a "pharmaceutical composition for therapeutic use . . . in combination with a pharmaceutically acceptable carrier." See, e.g., '829 Patent col.9 ll.55–67 (Claim 1) (emphasis added). In contrast, claim 10 and those claims that depend therefrom omit any reference to such a pharmaceutically acceptable carrier and, instead, recite "[a] pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings." '829 Patent col.10 ll.47–62 (Claim 10) (emphasis added). Thus, the distinction on which Defendant relies is already present in the language of the claims of the '829 Patent. The addition of "final dosage form" would result in the Court imposing an additional limitation that is not required by the claim language.

Even if Defendant's proposed construction was reasonable based solely on the words of the claims, this construction cannot survive a review of the rest of the specification. Defendant argues that the specification does support its proposed construction because the specification lists "suitable formulations" such as "injectable solutions; powders for injection . . . ; and tablets." (Resp. 16:9–10 (omission in original).) However, Defendant's Response Brief omits, by way of ellipses, the complete description of the "powders for injection" preferred embodiment. (See id.) Specifically, the specification states that "powders for injection" are actually "powders for injection, which may be reconstituted shortly before use by addition of Water for injection." '829 Patent col.5 ll.12–15 (emphasis added). Thus, not all "suitable formulations" are actually in a final form that can be administered to a patient; the "powder for injection" formulation requires additional steps before it can be injected into a patient. Not only is Defendant's proposed construction inconsistent with the specification, but it would also exclude this preferred embodiment. See Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1583 (Fed. Cir. 1996) (stating that a construction that excludes a preferred embodiment "is rarely, if ever, correct").

For these reasons, the Court declines to adopt Defendant's proposed construction.

2. *Plaintiffs' Proposed Construction*

In contrast to Defendant's proposed construction, Plaintiffs' proposed construction is consistent with both the words of the claims and with the words of the specification. Specifically, Plaintiffs' propose that the Court construe the phrase "pharmaceutical composition for therapeutic use" as "pharmaceutical composition for treating medical conditions."

Because Plaintiffs' proposed construction is consistent with the specification, the Court will adopt Plaintiff's proposed construction. Specifically, the specification discloses that this "pharmaceutical composition" can be used as "a rescue agent to counteract the action of DHFR inhibitors such as methotrexate"; it can be used "in the treatment of folate deficiency"; and,

finally, it "may be used in combination with 5-fluorouracil in the treatment of colorectal cancer . . .." '829 Patent col. 4, l.64–col.5, l.2. Accordingly, the specification expressly acknowledges that the claimed pharmaceutical composition is used to treat medical conditions.

3. *The Court's Construction*

For the reasons stated above, after looking first to the words of the claim and then the remaining parts of the specification, the Court finds that a person of ordinary skill in the art of organic chemistry would understand the '829 Patent to use the term "pharmaceutical composition for therapeutic use" as "a pharmaceutical composition suitable for treating medical conditions."

E. "Pharmaceutical composition for preparing medicaments for therapeutic use for the treatment of human beings"

Proposed Constructions

Spectrum	"[A] pharmaceutical composition from which can be prepared a medicine suitable for treating medical conditions in human beings"
Sandoz	"[A] pharmaceutical composition for preparing a final dosage form"

Much of the reasoning that applies to the construction of the phrase "[a] pharmaceutical composition for therapeutic use" also applies to the related phrase, "[a] pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings." Similar to Defendant's proposed construction in Section V.C.1, Defendant argues that this claim phrase also relates to "a final dosage form," specifically, to "a pharmaceutical composition for preparing a final dosage form." (Resp. 17:16–18, ECF No. 53.) However, for the reasons discussed above in Section V.C, the Court declines to include the "final dosage form" in its construction of this phrase. Also, for the reasons discussed above in Section V.C, the Court agrees with Plaintiffs' proposed construction.

/ / /

/ / /

1. *The Court's Construction*

Thus, after looking first to the words of the claim and then the remaining parts of the specification, the Court finds that a person of ordinary skill in the art of organic chemistry would understand the '829 Patent to use the term "pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings" as "a pharmaceutical composition from which can be prepared a medicine suitable for treating medical conditions in human beings."

F. The "pharmaceutically acceptable" Claim Terms

Proposed Constructions

"a pharmaceutically acceptable compound" (claim 1)	**Spectrum**	"a compound suitable for treating medical conditions which is not harmful to the recipient thereof"
	Sandoz	Plain Meaning
"a pharmaceutically acceptable composition" (claim 5)	**Spectrum**	"a composition suitable for treating medical conditions which is not harmful to the recipient thereof"
	Sandoz	Plain Meaning
"a pharmaceutically acceptable carrier" (claim 1, 5)	**Spectrum**	"a solid or liquid diluent that is compatible with the other ingredients of the formulation and is not harmful to the recipient thereof"
	Sandoz	Plain Meaning

A version of this claim term appears in independent claim 1 and independent claim 5.

1. *The Parties' Proposed Constructions*

Although Defendant initially requested that the Court construe this team, (see Antons Decl. Ex.3, at 1, ECF No. 50-3), Defendant asserts that the Court should give this term its plain meaning.[4]

/ / /

[4] Defendant has not provided the court with an explanation why it would request construction of a term and then simply assert that, essentially, no construction is required because the term should be given its plain meaning.

Plaintiffs, on the other hand, contend that for a compound/composition/carrier to be "pharmaceutically acceptable," it must be "suitable for treating medical conditions" and "not harmful to the recipient thereof." To support its proposed construction, Plaintiff provides only one citation to the intrinsic record. (Pls.' Br. 26:21–25, ECF No. 49.) The specification of the '829 Patent explains that this compound "may be used as a rescue agent to counteract the action of DHFR inhibitors such as methotrexate. It may also be used in the treatment of folate deficiency. In addition it may be used in combination with 5-fluorouracil in the treatment of colorectal cancer." '829 Patent col.4 l.64–col.5 l.4. This section of the written description does indicate that the intended purpose of the claimed compound is to treat human ailments. However, this section does not support a construction that would exclude all compounds that cause any harm to patients because, as Defendant notes, all pharmaceuticals have potential negative side effects. Furthermore, the Federal Circuit has previously rejected similar arguments in the context of pharmaceutical patents. Aventis Pharma S.A. v. Hospira, Inc., 675 F.3d 1324, 1330 (Fed. Cir. 2012) (declining to construe "suitable for infusion into patients" to include "efficacy, safety, and stability limitations" because the intrinsic record lacked support for such a construction"). Additionally, because of the inherent side effects, adopting Plaintiffs' proposed construction would only introduce further ambiguity into the scope of this claim term. Therefore, the Court will not adopt Plaintiffs' proposed "not harmful to the recipient" construction.

2. *The Court's Construction*

"The construction of claims is simply a way of elaborating the normally terse claim language in order to understand and explain, but not to change, the scope of the claims." Terlep, 418 F.3d at 1382. Furthermore, when the claim language is "clear on its face," then the Court's "consideration of the rest of the intrinsic evidence is restricted to determining if a deviation from the clear language of the claims is specified." Interactive Gift Exp., 256 F.3d at 1331. The

language of this disputed claim term is certainly clear on its face. Thus, after looking first to the words of the claim and then the remaining parts of the intrinsic record, the Court finds that a person of ordinary skill in the art of organic chemistry would understand the phrase "pharmaceutically acceptable," as used in the'829 Patent, to have its plain and ordinary meaning. For these reasons, the Court finds that this phrase, as used in claims 1 and 5, requires no further construction.

G. "consists essentially of"

Proposed Constructions

Spectrum	includes the following components, as well as components that do not materially affect the basic and novel characteristics of the claimed composition (such as impurities that do not impact the efficacy of the composition)
Sandoz	The specified materials and those that do not materially affect the basic and novel characteristic(s) of the composition

The phrase "consists essentially of" appears in Claim 1. Both parties acknowledge that the Federal Circuit has already determined that this term has an established meaning. (See Pls.' Br. 27:4–16, ECF No. 49; Resp. 26:4–19, ECF No. 53.) "By using the term 'consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention." PPG Indus. v. Guardian Indus. Corp., 156 F.3d 1351, 1354 (Fed. Cir. 1998). The "consisting of" transition phrase also permits "the inclusion of . . . impurities ordinarily associated with [the materials recited in the claim]." *Conoco, Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1360 (Fed. Cir. 2006).

1. The Parties' *Proposed Constructions*

Defendant simply requests that the Court construe this term in accordance with the well-established Federal Circuit case law discussed above. In contrast, although Plaintiff agrees that the Federal Circuit's endorsed definition of "consists essentially of" applies to claim 1 of the

’829 Patent, Plaintiff asserts that “the file history [of the ’829 Patent] adds to this definition. (Pl.’s Br. 27:9–16, ECF No. 49.) Specifically, Plaintiff asserts that the proper construction of this term would also expressly state that any “impurities that do not impact the efficacy of the composition” may also be present in the claimed pharmaceutical composition. (Id. at 27:13–16.) Plaintiff supports this assertion by relying on an Appeal Brief submitted during prosecution which provides:

> The term “consists essentially of” has a well-known meaning in patent law; see e.g., MPEP § 2111.03 (The scope of the claim is limited "to the specified materials or steps ‘and those that do not materially affect the basic and novel characteristic(s)’.”)
>
> It is apparent that these claims are directed to compositions in which the (6R) diastereoisomer is present in the specified amount; and that, for example, excess (6R) diastereoisomer would be excluded as would be additives destroying pharmaceutical purity.

(Antons Decl. Ex. 6, at 20, ECF No. 50-6.) Plaintiffs argue that this passage supports their construction because

> [t]he example provided to the examiner was in the form of what would be excluded. Plaintiffs’ construction incorporates this language that impurities (“additives”) are permitted as long as those impurities do not increase the recited amount of the (6R) diastereoisomer or impact the efficacy of the composition (“destroying pharmaceutical purity”).

(Pls.’ Br. 28:2–6.)

The Court disagrees that this portion of the prosecution history warrants the construction that Plaintiffs request. First, this section of the appeal brief solely recognizes that many of the claims list a specific amount of the (6R) diastereoisomer that must be present and that a pharmaceutical composition that included an amount of the (6R) diastereoisomer in excess of those specified amounts would not be covered by the claims of the ’829 Patent. Implying from this language that other impurities would be covered by the claims is a leap that the Court is neither willing nor required to make. In fact, the Federal Circuit has expressly noted that when

the specification is silent as to the effect of a given component, whether the presence of that additional component has a "material effect" on the claimed invention is not a matter of claim construction but is, instead, an issue for the factfinder as part of its infringement determination. See, e.g., PPG Indus., 156 F.3d at 1354–55.

Here, the Court does not doubt that there are certain impurities that are "ordinarily associated" with the claimed composition that would be covered by the'829 Patent. See Conoco, Inc., 460 F.3d at 1360 ("[I]mpurities that a person of ordinary skill in the relevant art would ordinarily associate with a component on the 'consisting of' list do not exclude the accused product or process from infringement."). However, the parties have not pointed to any specific impurity. As such, the Court is unable to determine whether the specification contemplates whether these impurities would have a material effect on the claimed composition. Furthermore, Plaintiffs have failed to provide the Court with any reference to the specification from which the Court could determine whether the general category of "impurities" has a material effect. Accordingly, the Court declines to adopt Plaintiffs' requested construction and will leave the question of whether a given impurity, that will presumably be identified at trial, has a material effect on the claimed composition such that the presence of that impurity in an accused composition renders that accused composition non-infringing.

2. *The Court's Construction*

After looking first to the words of the claim and then the remaining parts of the specification, the Court finds that a person of ordinary skill in the art of organic chemistry would understand the'829 Patent to use the phrase "consists essentially of" as meaning "the specified materials and those that do not materially affect the basic and novel characteristic(s) of the composition."

/ / /

/ / /

H. The "Multiple Dose" or "4,000 mg (4 grams)" Claim Terms[5]

Proposed Constructions

"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" (claim 5)	**Spectrum**	"the pharmaceutically acceptable composition is present in the claimed pharmaceutical composition in an amount of 4,000 mg or more"
	Sandoz	"the composition being present in a final unit dosage form in an amount sufficient to provide multiple doses of the two-component combination of non-negligible amounts of each of the (6S) and (6R) diastereoisomers" The "multiple dose" claim terms should retain the "per dose" limitation
"said mixture of (6S) and (6R) diastereoisomers being present in said pharmaceutical composition in an aggregate quantity at least sufficient to provide multiple doses of said mixture in an amount of 2000 mg per dose" (claim 10)	**Spectrum**	"the mixture of (6S) and (6R) diastereoisomers of leucovorin is present in the claimed pharmaceutical composition in an amount of 4,000 mg or more"
	Sandoz	"a total amount of the two-component combination consisting of non-negligible amounts of each of the (6S) and (6R) diastereoisomers, sufficient to provide multiple doses of the two-component combination" The "multiple dose" claim terms should retain the "per dose" limitation

Some form of these "4,000 mg (4 grams)" or "multiple dose" claim terms appears in independent claims 5 and 10.

1. *The Parties' Proposed Constructions*

Plaintiffs urge the Court to construe these claims to require that the mixture of (6S) and (6R) diastereoisomers is present in an amount of at least 4,000 mg. In response, Defendant first asserts that Plaintiffs' proposed construction would impermissibly eliminate the requirement

[5] Plaintiffs refer to this group of claim terms as the "4,000 mg (4 grams)" claim terms, (see Pls.' Br. 28:8), and Defendant refers to this group of claim terms as the "multiple dose" claim terms, (see Resp. 22:22–23).

that the mixture be present in an amount of at least 2,000 mg per dose. Defendant also incorporates the "final dosage form" and the "non-negligible" language into its proposed constructions. As discussed above, the Court finds that the intrinsic record does not support the inclusion of these phrases. Thus, the Court will not adopt the portions of Defendant's proposed constructions that incorporates these phrases.

However, the Court also concludes that Plaintiffs' proposed construction is improper because it impermissibly ignores the "per dose" limitation recited in claims 5, 10 and the claims that depend therefrom. Plaintiffs contend that providing "multiple doses" of the mixture "in an amount of 2000 mg per dose" necessarily requires that the claimed composition contain, at minimum, 4,000 mg of the (6S) and (6R) mixture. (Pls.' Br. 28:20–29:2, ECF No. 49.) Plaintiffs argue that their proposed construction merely "incorporate[s] [the "2000 mg per dose" limitation] into their proposed construction with an explicit requirement that the claimed composition must contain 4,000 milligrams or more of the (6S)/(6R) mixture." (Reply 19:24–20:2, ECF No. 56.)

Plaintiffs also attempt to rely on the prosecution history to further support their proposed construction. True enough, during the prosecution of the '829 Patent, the inventors stated that the claims required a minimum of four grams of the (6S)/(6R) mixture. (Antons Decl. Ex. 6, at 26, ECF No. 50-6.) Despite Plaintiffs' arguments to the contrary, these statements in the prosecution history cannot overcome the words of claims 5 and 10. See Phillips, 415 F.3d at 1317 (cautioning that the prosecution history "often lacks the clarity of the specification and thus is less useful for claim construction purposes"). This prosecution history argument is also unpersuasive in light of the differences between the words of independent claims 5 and 10 and dependent claims 6 and 11. See id. at 1314 ("Other claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment as to the meaning of a claim term."). Specifically, both claims 6 and 11 expressly state that the "mixture of (6S) and

(6R) diastereoisomers is present in said composition in an amount of at least about 10 grams." '829 Patent col.10 ll.25–28 (Claim 6), col.10 ll.63–67 (Claim 11). If the inventors had wanted claims 5 and 10 to incorporate a minimum of 4000 mg, or 4 grams, the inventors could have worded claims 5 and 10 similarly to claims 6 and 11. In light of the applicant's decision to incorporate different words in these claims, the language of Claims 6 and 11 establish that a proper construction of this claim term must retain the "per dose" language.

2. *The Court's Construction*

As discussed above, the Court concludes that neither party has provided a correct construction for this disputed claim term. "The construction of claims is simply a way of elaborating the normally terse claim language in order to understand and explain, but not to change, the scope of the claims." Terlep, 418 F.3d at 1382. Furthermore, when the claim language is "clear on its face," then the Court's "consideration of the rest of the intrinsic evidence is restricted to determining if a deviation from the clear language of the claims is specified." Interactive Gift Exp., 256 F.3d at 1331. The language of this disputed claim term is certainly clear on its face. This phrase merely calls for a pharmaceutical composition capable of providing two or more doses of the claimed mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg, or two grams, at minimum, per dose. In contrast, claim 10 provides that the pharmaceutical composition must contain a sufficient amount of the (6S) and (6R) mixture to provide "at least" 2000 mg, or two grams, per dose.

Thus, after looking first to the words of the claim and then the remaining parts of the intrinsic record, the Court finds that a person of ordinary skill in the art of organic chemistry would understand the phrase "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 used in the'829 Patent, to have its plain and ordinary meaning. The words of the claims and the remaining parts of the specification do not support the construction asserted by

either party. Rather, "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" simply requires that the pharmaceutical composition contains enough of the (6S)/(6R) mixture to provide two or more doses of, at minimum, 2000 mg per dose of the mixture. For these reasons, the Court finds that this phrase, as used in claims 5 and 10, requires no further construction.

I. Preamble of Claim 13: "The pharmaceutical composition for therapeutic use for the treatment of human beings prepared from the composition of claim 11"

Proposed Constructions

Spectrum	"A composition suitable for treating medical conditions in human beings prepared from the composition recited in claim 11"
Sandoz	This term improperly depends from claim 11

1. Claims 13 and 14 are both dependent claims.

The Patent Act permits applicants to draft a claim that incorporates by reference all the limitations from a previously stated claim, but requires that this "dependent" claim must further narrow the scope of the claim from which the claim depends. 35 U.S.C. § 112(d) ("[A] claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.") The Federal Circuit has instructed that "[t]o establish whether a claim is dependent upon another, [courts] examine[] if the new claim both refers to an earlier claim and further limits that referent." Monsanto Co. v. Syngenta Seeds, Inc., 503 F.3d 1352, 1357 (Fed. Cir. 2007) (citing 35 U.S.C. § 112(d)). However, when engaging in this analysis, courts must be mindful that "[a] claim's status as dependent or independent depends on the substance of the claim in light of the language of § 112, ¶ 4, and not the form alone." Id. at 1357–58.

Here, Plaintiffs argue that both claim 13 and claim 14 are independent claims, despite the references to claim 11 and claim 10, respectively. Plaintiffs contend that these claims simply

"incorporate[] the composition claim[s] by reference, thereby avoiding having to rewrite all of the limitations in claims 10 and 11." (Pls.' Br. 21:11–14, ECF No. 49.) In contrast, Defendant asserts that the Court should construe these terms as dependent claims because claim 13 refers to claim 11 and claim 14 refers to claim 10.

Although not cited by the parties, the Court finds the Federal Circuit's decision in Monsanto Co. v. Syngenta Seeds, Inc. particularly instructive on this issue. In Monsanto Co. v. Syngenta Seeds, Inc., the Federal Circuit was confronted with whether a claim was a dependent or an independent claim when the claim referred to another claim and was written "in a somewhat unusual format." 503 F.3d at 1357–58. Specifically, claim 4 recited: "A process comprising obtaining progeny from a fertile transgenic plant obtained by the process of claim 1 which comprise said DNA." Id. at 1355 (quoting United States Patent No. 5,538,880 (filed May, 26, 1994)). Despite the plaintiff's urging to the contrary, the Federal Circuit concluded that claim 4 depended from claim 1 because the additional step that claim 4 added could be performed only after the completion of the steps recited in claim 1. Id. at 1358 ("In other words, the additional fourth step of obtaining progeny depends on the performance of the process comprising the three steps recited in claim 1."); see also Maury Microwave. Inc. v. Focus Microwaves, Inc., 10-cv-03902-MMM-JCGX, 2012 WL 9161988, at *32–33 (C.D. Cal. July 30, 2012) (concluding that the claims that referred to another claim were dependent on the referenced claim because the steps of the referenced claim had to be performed before the step in the disputed claim could commence).

Claims 13 and 14 of the '829 Patent are written in a similarly "unusual format." Claim 13 of the '829 Patent recites: "[A][6] pharmaceutical composition for therapeutic use for the

[6] The originally issued claim 13 recited "The pharmaceutical composition . . .." '829 Patent col.11 l.7 (emphasis added). However, the '829 Patent includes a Certificate of Correction, dated October 2, 2012, which provides that claim 13 should recite "A pharmaceutical composition . . .."

treatment of human beings prepared from the composition of claim [11][7] in a form selected from the group consisting of injectable powers for injection which can be reconstituted shortly before use by addiction of water for injection; and tablets." '829 Patent col.11 l.7–col.12 l.2 (footnotes added). Similar to the claim in Monsanto, the composition in claim 13 can be created only after the composition in claims 10 and 11 are created; the composition of claim 13 depends on the prior creation of the compositions recited in claims 10 and 11. Accordingly, claim 13 is a dependent claim that depends from claim 11, which depends from claim 10.

Claim 14 recites: "The pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings[8] as defined in claim 10 wherein said composition is produced as a result of separation by differential solubility in a polar solvent of a (6S) diastereoisomer from an initial mixture containing equal amounts of (6S) and (6R) diastereoisomers." '829 Patent col.12 ll.3–8 (footnote added). Again, this composition can only be created after the composition covered by claim 10 is first created. Therefore, claim 14 is also a dependent claim that depends from claim 10.

In addition, the prosecution history further supports the Court's conclusion that claims 13 and 14 are dependent claims. In fact, the application expressly provides for fourteen total claims of which only three are independent claims. (Keane Decl. Ex. 12, at 7, ECF No. 54-12.) Neither party disputes that these three independent claims consist of claim 1, claim 5, and claim 10. According to the patent application, the remaining eleven claims were claims that depended from one of these three independent claims. Thus, the prosecution history also persuades the Court, as Defendant urges, that claims 13 and 14 are dependent claims.

---

[7] The originally issued claim 13 refers to claim 12. However, the '829 Patent includes a Certificate of Correction, dated May 6, 2003, that recognizes that claim 13 should, in fact, refer to claim 11, rather than claim 12.

[8] The originally issued claim 14 recited "The pharmaceutical composition for therapeutic use for the treatment of human beings . . .." '829 Patent col.12 l.3-4. However, the '829 Patent includes a third Certificate of correction, dated January 22, 2013, which provides that claim 14 should recite "The pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings . . .."

2. Validity of claims 13 and 14

"A patent shall be presumed valid." 35 U.S.C. § 282(a). "To overcome this presumption of invalidity, the party challenging a patent must prove facts supporting a determination of invalidity by clear and convincing evidence." Schumer v. Lab Computer Sys., Inc., 308 F.3d 1304, 1315 (Fed. Cir. 2002); see also 35 U.S.C. § 282(a) ("The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity.").

Defendant asserts that, not only are claims 13 and 14 dependent claims, but also that these claims are invalid because they improperly depend from claims 10 and 11. (See generally Resp. 19:26–22:21, ECF No. 53.) Specifically, Defendant contends that claims 13 and 14 are invalid because the dependent claims and the independent claims from which they depend relate to "non-overlapping subject matter." (Resp. 20:15–17.)

Although this topic is infrequently litigated, the Federal Circuit's decision in Pfizer, Inc. v. Ranbaxy Laboratories appears to govern this issue. 457 F.3d 1284, 1291 (Fed. Cir. 2006). In Pfizer, the disputed dependent claim read: "The hemicalcium salt of the compound of claim 2." Id. However, claim 2, from which the disputed claim depended, claimed only atorvastatin acid and did "not include the pharmaceutically acceptable salts of atorvastatin acid."[9] Id.

Here, claim 13 suffers from a similar defect. One claim covers a composition that can be used to prepare a medicament and the other claims the actual medicament. Specifically, Claim 11, from which claim 13 depends, claims a composition <u>for preparing</u> a medicament. '829 Patent col.10 ll.63–65 ("The pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings . . .." (emphasis added)). In contrast, claim 13 does not recite a composition that can be used to prepare a medicament. See '829 Patent col.11

[9] The Court noted that, "[t]heoretically, a claimed acid could be liberally construed to include the corresponding salts. But here, given the absence of the 'pharmaceutically acceptable salts thereof' language which was used in claim 1, the intrinsic evidence would not have supported such an interpretation of claim 2." Pfizer, 457 F.3d at 1291 n.6.

ll.7–8. Rather, claim 13 claims the medicament itself that can be used for the actual treatment of human beings. '829 Patent col.11 ll.7–8 ("[A] pharmaceutical composition for therapeutic use for the treatment of human beings . . .") The distinctions between the language of these two claims is fatal to claim 13. As in Pfizer, these two claims "deal with non-overlapping subject matter" and claim 13 must be invalid.

Because of the January 22, 2013 Certificate of Correction, claim 14 does not suffer from this defect. This Certificate of Correction expressly alters the language of claim 14 to recite: "The pharmaceutical composition for preparing medicaments for therapeutic use in the treatment of human beings . . ." Thus, the subject matter of dependent claim 14 overlaps with claim 10, from which claim 14 depends, because claim 10 also recites "[a] pharmaceutical composition for preparing medicaments . . ." '829 Patent col.10 ll.47–48. Accordingly, the Court concludes that Defendant has failed to carry its burden of establishing, by clear and convincing evidence, that claim 14 is invalid.

3. *The Court's Construction*

For the reasons discussed above, the Court concludes that both claim 13 and claim 14 are drafted in dependent format. Claim 13 depends from claim 11, which in turn depends from claim 10. Claim 14 depends from claim 10.

In addition, the Court holds that claim 13 is invalid. However, Defendant failed to carry its burden of establishing the invalidity of claim 14 by clear and convincing evidence; therefore, the Court cannot conclude that claim 14 is invalid.

VI. CONCLUSION

IT IS HEREBY ORDERED that the proposed construction of the nine (9) terms submitted by the parties are construed as contained within this Order. The Court construes the primary nine (9) disputed claim terms in U.S. Patent No. 6,500,829 as follows:

/ / /

"mixture"	Plain and ordinary meaning
the "percentage" claim terms	Plain and ordinary meaning
"the balance of said composition consisting of the (6R) diastereoisomer"	the remaining amount of the mixture of (6S) and (6R) diastereoisomers is the (6R) diastereoisomers, and any impurities normally associated with the mixture of (6S) and (6R) diastereoisomers
"pharmaceutical composition for therapeutic use"	a pharmaceutical composition suitable for treating medical conditions
"pharmaceutical composition for preparing medicaments for therapeutic use for the treatment of human beings"	a pharmaceutical composition from which can be prepared a medicine suitable for treating medical conditions in human beings
"consists essentially of"	"the specified materials and those that do not materially affect the basic and novel characteristic(s) of the composition"
the "multiple dose" or "4,000 mg (4 grams)" claim terms	Plain and ordinary meaning; the pharmaceutical composition must contain enough of the (6S)/(6R) mixture to provide two or more doses of, at minimum, 2000 mg per dose of the mixture

IT IS FURTHER ORDERED that claims 13 and 14 are both dependent claims. Claim 13 depends from claim 11. Claim 14 depends from claim 10.

IT IS FURTHER ORDERED that claim 13 is invalid as improperly dependent from claim 11.

IT IS FURTHER ORDERED that this case shall be referred to Magistrate Judge Nancy J. Koppe for the setting of the Post-Claim Construction Order Settlement Conference pursuant to Local Rule 16.1-19(b).

DATED this 8th day of January, 2014.

NUNC PRO TUNC DATE: December 31, 2013.

Gloria M. Navarro
United States District Judge