NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

UNITED THERAPEUTICS CORP., Plaintiff, v. SANDOZ, INC., et al., Defendants.	Civil Action No. 3:12-CV-01617 **MEMORANDUM DECISION & ORDER**

SHERIDAN, U.S.D.J.

In this patent infringement case, the parties dispute the construction of several claim terms in U.S. Patent Nos. 5,153,222 ("the '222 patent") and 7,999,007 ("the '007 patent"). Plaintiff United Therapeutics Corp. ("UTC") holds approved New Drug Application No. 21-272 for Treprostinil Sodium Injection, which UTC markets and sells as REMODULIN. The case relates to the proposed marketing and sale by Defendant Sandoz, Inc. ("Sandoz") of a generic copy of the REMODULIN Injection product sold by UTC. REMODULIN is a product approved by the FDA for the treatment of pulmonary arterial hypertension, a rare, debilitating, and potentially fatal disease. UTC has listed the '222 patent, the '007 patent, and a third patent, U.S. Patent No. 6,765,117, in *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book") in connection with REMODULIN. UTC filed the present patent infringement action under the Hatch-Waxman provisions of the patent law, 35 U.S.C. § 271(e), asserting that Sandoz's filing of its Abbreviated New Drug Application ("ANDA") for a generic treprostinil product infringes the three patents listed in the Orange Book. Only terms from the

‘222 and ‘007 patents are in dispute. After reviewing the parties’ respective submissions and conducting a *Markman* hearing on May 20, 2013, the Court construes the disputed claim terms as set forth in subsection III below. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967 (Fed. Cir. 1995) (*en banc*), *aff’d* 517 U.S. 370 (1996).

I. BACKGROUND

A. The ‘222 Patent

The ‘222 patent, is entitled “Method of treating pulmonary hypertension with benzi[n]dine prostaglandins.” The ‘222 patent has two claims, both of which are independent claims directed to a “method of treating pulmonary hypertension in a patient.” The methods claimed in the patent for the treatment of pulmonary hypertension are by administering an “effective pulmonary hypertension treatment amount” of treprostinil (claim 1), or a pharmaceutically acceptable salt thereof (claim 2). (‘222 patent at 6:51-63). Representative claim 1 reads as follows:

> A method of treating pulmonary hypertension in a patient, which comprises administering to said patient an effective pulmonary hypertension treatment amount of the compound 9-deoxy-2',9α-methano-3-oxa-4,5,6-trinor-3,7-(1',3'-interphenylene)- 13,14-dihydro-prostaglandin F1.

(*Id*. at 6:53-57). The parties dispute the meaning of the term “pulmonary hypertension” as used in both claims 1 and 2.

B. The ‘007 Patent

The ‘007 patent is entitled “Buffer solutions having selective bactericidal activity against gram negative bacteria.” The ‘007 patent is directed generally to improved methods or pharmaceutical preparations for administering treprostinil to a patient. More specifically, the ‘007 patent is directed to compositions, including treprostinil, with a glycine buffer having a high

pH and methods for killing and inhibiting the growth of bacteria using such compositions. The '007 patent specification explains that "[t]he use of buffers to maintain a pH and solubilize or dilute active pharmaceutical agents ("APIs") before administration (e.g., by injection) is routine;" however, many buffers "contain components that maintain a neutral pH and foster microbial growth, which can lead to sepsis and other undesirable infection-related complications." ('007 patent at 1:26-31). The '007 patent claims an invention that addressed that problem through an improved pharmaceutical preparation or method of administering treprostinil with a high pH buffer solution that reduced the likelihood of those infections.

There are 26 claims in the '007 patent. UTC is asserting claims 1-5, 7-17 and 19-26 ("Asserted Claims"). Claims 1-5, 7-10 and 21 are drawn to methods of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria in a pharmaceutical preparation. ('007 patent at 7:58-8:51). Independent claim 1 is representative of this group of claims and reads as follows:

> A method of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria in a pharmaceutical preparation comprising an active agent selected from the group consisting of treprostinil and treprostinil sodium, the method comprising supplying the active agent with a buffer comprising glycine and having a pH of greater than 10 with low buffer capacity.

(*Id.* at 7:58-64).

Claims 11-17 and 19-20 are drawn to methods of reducing the occurrence of blood stream infections in mammals. (*Id.* at 8:20-40, 8:43-51). Independent claim 11 is representative of the second group of claims and reads as follows:

> A method of reducing the occurrence of blood stream infections in a mammal being treated with an active agent comprising administering to the mammal the active agent with a buffer comprising glycine and having a pH of greater than 10, wherein the active agent is selected from the group consisting of treprostinil and treprostinil sodium, and wherein the administration reduces the gram negative bacteria and inhibits the growth of gram positive bacteria.

(*Id*. at 8:20-27).[1]

Several dependent claims are further directed to the pH of the claimed glycine buffer. Dependent claim 4 is representative and reads as follows:

> 4. The method of claim 1, wherein the buffer has a pH between about 10 to about 12 with low buffer capacity.

(*Id.* at 8:3-4).

The parties dispute the meaning of the following four claim terms from the '007 patent:

- "A method of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria in a pharmaceutical preparation" as used in claim 1;
- "the method comprising supplying the active agent with a buffer comprising glycine and having a pH of greater than 10 with low buffer capacity" as used in claim 1;
- "a pH between about 10 to about 12" as used in claims 4, 16 and 24; and
- "wherein the administration reduces the gram negative bacteria and inhibits the growth of gram positive bacteria" as used in claim 11.

II. LEGAL STANDARDS FOR CLAIM CONSTRUCTION

There is a two-step analysis for determining patent infringement: "first, the court determines the meaning of the disputed claim terms, then the accused device is compared to the claims as construed to determine infringement." *Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 804 (Fed. Cir. 2007) (citation omitted). When the court engages in claim construction to determine the meaning of disputed claim terms, it is decided as a matter of law. *Markman v.*

[1] Claims 22, 23, 25 and 26 are composition claims. (*Id.* at 8:52-63). The parties do not dispute any terms contained in these claims.

Westview Instruments, 517 U.S. 370, 372 (1996). It is well established that "the construction of a patent, including terms of art within its claim, is exclusively within the province of the court." *Id.*

When construing claims, the court must focus on the claim language. As explained by the Federal Circuit:

> 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. Attending this principle, a claim construction analysis must begin and remain centered on the claim language itself, for that is the language the patentee has chosen to particularly point out and distinctly claim the subject matter which the patentee regards as his invention.

Innova/Pure Water, Inc. v. Safari Water Filtration Sys., 381 F.3d 1111, 1115-16 (Fed. Cir. 2004) (citations omitted). When looking at the words of a claim, the words "are generally given their ordinary and customary meaning," which has been defined as "the meaning that the term 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).

The Federal Circuit has counseled:

> It is the person of ordinary skill in the field of the invention through whose eyes the claims are construed. Such person is deemed to read the words used in the patent documents with an understanding of their meaning in the field, and to have knowledge of any special meaning usage in the field. The inventor's words that are used to describe the invention – the inventor's lexicography – must be understood and interpreted by the court as they would be understood and interpreted by a person in that field of technology. Thus the court starts the decision making process by reviewing the same resources as would that person, viz., the patent specification and prosecution history.

Id. at 1313 (quoting *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998)). Those resources, called intrinsic evidence, include the claim language, the specification, and the prosecution history. *See id.* at 1314.

However, when intrinsic evidence alone does not resolve the ambiguities in a disputed claim term, extrinsic evidence – evidence that is outside the patent and prosecution history – may also be used to construe a claim. *See id.* at 1317; *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582-83 (Fed. Cir. 1996). "[E]xtrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art" may be consulted; for example, expert testimony, dictionaries, and treatises. *Id.* at 1314. However, when a court relies on extrinsic evidence to construe a claim, the court should be guided by the principle that extrinsic evidence may never conflict with intrinsic evidence, because courts "have viewed extrinsic evidence in general as less reliable than the patent and its prosecution history in determining how to read claim terms." *Id.* at 1319. Thus, a court should take care to "attach the appropriate weight to be assigned to those sources." *Id.* at 1322-24.

III. ANALYSIS

Set forth below are the parties' proposed constructions along with the primary arguments advanced in support of the proposed constructions. In formulating its own constructions of the disputed terms, the Court considered all of the arguments in the parties' written submissions, as well as those made at oral argument.

A. '222 Patent

Term 1: "pulmonary hypertension" ('222 patent, claims 1 and 2)

The term "pulmonary hypertension" is found in claims 1 and 2 of the '222 patent. Claims 1 and 2 recite "[a] method of treating pulmonary hypertension in a patient, which

comprises administering to said patient an effective pulmonary hypertension treatment amount of" treprostinil or a pharmaceutically acceptable salt of treprostinil, respectively. The parties' proposed constructions are:

UTC's Construction	Sandoz's Construction
Plain and ordinary meaning. To the extent the Court determines that this term requires construction, UTC proposes the following: "primary and secondary pulmonary hypertension as ordinarily understood by clinicians at the time of invention"	"Increased resistance to pulmonary blood flow resulting in greater pressure in the circulation for any particular flow, which includes both primary and secondary pulmonary hypertension."

As indicated above, UTC primarily argues that the term "pulmonary hypertension" needs no construction because its definition is readily apparent to a person of ordinary skill in the art ("POSITA"), and alternatively argues that the Court should adopt what it considers to be "the explicit definition" set forth in the '222 patent. Plaintiff' Opening Claim Construction Brief [D.E. 68] ("UTC Br.") at 8. Sandoz, too, argues that the Court should adopt "the explicit definition in the specification," but it points to a "definition" that is quite different than the one proposed by UTC. Defendant's Opening Claim Construction Brief [D.E. 67] ("Sandoz Br.") at 18. Sandoz relies in large part[2] on the following passage from the specification:

> When the resistance to pulmonary blood flow increases, the pressure in the circulation is greater for any particular flow. This is referred to as pulmonary hypertension. Generally, pulmonary hypertension is defined through observations of pressures above the normal range pertaining in the majority of people residing at the same altitude and engaged in similar activities.
>
> Most often pulmonary hypertension is a manifestation of an obvious or explicable increase in resistance, such as obstruction to blood flow by pulmonary emboli, malfunction of the heart's valves or muscle in handling

[2] Sandoz wrote that the inventors "*defined* 'pulmonary hypertension' in the '222 specification" by way of the *entire quoted passage. See* Sandoz Br. at 17 (emphasis added).

> blood after its passage through the lungs, diminution in pulmonary vessel calibre as a reflex response to hypoventilation and low oxygenation, or a mismatch of vascular capacity and essential blood flow, such as shunting of blood in congenital abnormalities or surgical removal of lung tissue. Such pulmonary hypertension is referred to as secondary hypertension.
>
> There remain some cases of pulmonary hypertension where the cause of the increased resistance is as yet inexplicable. They are described as primary pulmonary hypertension (PPH) and are diagnosed by and after exclusion of the causes of secondary pulmonary hypertension. . . .
>
> We have now discovered that within the class of benzindene prostaglandins described in the U.S. Patent, there is a sub-class of compounds of formula (I) as defined hereinbefore which are suitable for use in the treatment of pulmonary hypertension. The term "pulmonary hypertension" is used herein to include both primary and secondary pulmonary hypertension as ordinarily understood by clinicians (vide supra).

('222 patent at 1:24-45, 2:1-8).

From this, Sandoz proposes that "pulmonary hypertension" should be construed to mean "increased resistance to pulmonary blood flow resulting in greater pressure in the circulation for any particular flow, which includes both primary and secondary pulmonary hypertension." Sandoz argues that its proposed definition is: (1) consistent with the usage of the term in the specification; (2) consistent with the ordinary and customary meaning accorded the term by a POSITA; and (3) preferable to UTC's construction because Sandoz's definition does not "put off determining the precise meaning" of the term until trial as Sandoz argues UTC's definition would.

UTC's primary argument is that "pulmonary hypertension" needs no construction because it is not ambiguous, overly technical, or unclear; UTC argues that the term was used in common parlance and readily understood by POSITAs at the time of the invention. UTC argues that Sandoz's proposed construction will confuse the issues by "introducing ambiguity and undue breadth to an understood term" by encompassing "<u>any</u> 'increased resistance' or <u>any</u>

'greater pressure' as compared to some undefined norm." UTC Br. at 10, 13 (emphasis in original).[3] UTC further argues that Sandoz's construction improperly imports selective language from the specification – "a single passage plucked from the background" – while ignoring its context. *Id.* at 8, 10.

UTC argues alternatively that if the Court chooses to construe "pulmonary hypertension" it should use what UTC considers to be (rather than what Sandoz considers to be) the "express definition" set out in the specification; UTC's "express definition" is the last sentence of the passage quoted above, *i.e.* the passage which Sandoz argues is the definitional passage from the specification. The sentence reads: "The term 'pulmonary hypertension' is used herein to include both primary and secondary pulmonary hypertension as ordinarily understood by clinicians (vide supra)." UTC argues that the phrase "is used herein" shows that the patentees were defining a term. Based on this, UTC proposes the following construction: "primary and secondary pulmonary hypertension as ordinarily understood by clinicians at the time of invention". UTC further argues that in light of the "as ordinarily understood by clinicians" language, Sandoz's construction misses the mark because clinicians would not have considered *any* increase in resistance or *any* increase in pressure to constitute pulmonary hypertension. Dipping into extrinsic evidence, UTC argues that at the time of the invention, patients with pulmonary hypertension were generally clinically defined by "specific hemodynamic criteria . . . [which] generally included a mean pulmonary arterial pressure of greater than 25 mm Hg." *See* UTC Br. at 14.[4]

[3] UTC argues that the proposed construction "could encompass wide swaths of the population who do not suffer from the disease [of pulmonary hypertension]." At oral argument, UTC suggested that healthy people who are exercising, mountain climbing, or who have been alarmed or frightened would all fall within the ambit of the proposed construction.

[4] UTC cites, *inter alia*, Moore et al., *The relationship between Pulmonary Artery Pressure and Pulmonary Artery Diameter in Pulmonary Hypertension*, 39 Clinical Radiology 486-489 (1988); Chapman et al., *Prognostic and*

Claim Construction

The Court is not satisfied with either of the parties' proposed constructions, and the Court believes that this disputed term should be defined. In formulating a construction of "pulmonary hypertension", the Court is guided by the principle that ordinarily the inventor's express definition of a claim term prevails. *See, e.g.*, *Int'l Rectifier Corp. v. IXYS Corp.,* 361 F.3d 1363, 1373 (Fed. Cir. 2004). Here the parties have each proposed a competing "express definition." The Court agrees with Sandoz that the entire passage it cited is definitional in nature. It is telling that UTC cites part of the same passage in its own definition. At oral argument the Court proposed a definition to the parties that attempted to summarize and incorporate all of the definitional statements from the passage. The Court now adopts that construction, because it is a more complete expression of the inventors' definition of "pulmonary hypertension" than what was proposed by either party, and because it incorporates the proposals of both parties. The Court's construction of "pulmonary hypertension" is as follows:

> increased resistance to pulmonary blood flow resulting in greater pressure in the circulation for any particular flow, which is generally defined through observations of pressures above the normal range pertaining in the majority of people residing at the same altitude and engaged in similar activities, and which includes both primary and secondary pulmonary hypertension as ordinarily understood by clinicians.

While UTC criticizes the use of the language "increased resistance to pulmonary blood flow resulting in greater pressure in the circulation for any particular flow," the Court rejects UTC's argument because the language is part of the inventor's explicit definition of the disputed term. *See* '222 patent at 1:24-25. In addition, UTC's concern that Sandoz has "cherry-picked" language from the specification misses the context in which it appears in the patent; the Court

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Therapeutic considerations in clinical primary pulmonary hypertension, 84 Respiratory Medicine 489-494 (1990); Chin and Rubin, *Pulmonary Arterial Hypertension*, 51 J. Am. College Cardiology, No. 16, at 1527-1538 (2008).

finds that taken as a whole the construction is reasonable and that the inclusion of the phrases "defined through observations of pressures" and "as ordinarily understood by clinicians" ameliorates UTC's concern that the construction will be improperly divorced from clinicians' perspectives. Accordingly, the Court's proposed construction is adopted.

B. '007 Patent

Term 2: "A method of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria in a pharmaceutical preparation" ('007 patent, claim 1)

The parties dispute two "terms" in claim 1 of the '007 patent. Claim 1, with the two disputed claim terms underlined, reads as follows:

> A method of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria in a pharmaceutical preparation comprising an active agent selected from the group consisting of treprostinil and treprostinil sodium, the method comprising supplying the active agent with a buffer comprising glycine and having a pH of greater than 10 with low buffer capacity.

The Court now addresses the first of these two disputed terms – "[a]method of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria in a pharmaceutical preparation." The parties' proposed constructions are:

UTC's Construction	Sandoz's Construction
This term is an affirmative limitation that should be accorded its plain and ordinary meaning. To the extent the Court determines that this term requires construction, UTC proposes the following: "A method of preferentially reducing gram negative bacteria and preventing the increase of gram positive bacteria in a pharmaceutical preparation"	"A method of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria that are present in a pharmaceutical preparation prior to the step of supplying the active agent with a buffer"

UTC argues that the term needs no construction because all of the words standing on their own or in the context of the claims are readily understood and apparent to a person of ordinary skill in the art. UTC argues in the alternative that should the Court decide to construe the terms, UTC's proposed definitions are consistent with their plain and ordinary meaning and with the intrinsic evidence in the patent specification. In summary, UTC's construction of the first term interprets the term "selectively killing" to mean "preferentially reducing" gram negative bacteria, and "inhibiting the growth of" is interpreted to mean "preventing the increase of" gram positive bacteria.

Sandoz's proposed construction of the first disputed term in claim 1 is illustrated as follows, where the underlined phrases indicate Sandoz's proposed additions:

> A method of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria <u>that are present</u> in a pharmaceutical preparation <u>prior to the step of supplying the active agent with a buffer</u> comprising an active agent selected from the group consisting of treprostinil and treprostinil sodium[.]

Sandoz argues that its addition to the preamble of the phrases "that are present" and "prior to the step of supplying the active agent with a buffer" is consistent with the plain language of the claim because in order for bacteria to be killed and inhibited they must be present in the pharmaceutical preparation prior to the step of supplying the active agent with a buffer. Sandoz contends that this is the only reasonable interpretation of the claim language. Sandoz argues that UTC's proposed construction of the preamble language is ambiguous because it "leaves unresolved whether claim 1 requires the presence of bacteria in the pharmaceutical preparation prior to the step of supplying the buffer to kill (and inhibit the growth of) the bacteria in the pharmaceutical preparation." Sandoz Brief at 25; *see also id.* at 27.

UTC takes issue with Sandoz's proposed construction because it says that the words in the disputed terms need no interpretation and because Sandoz's proposed additions would alter the meaning of the claim terms. In UTC's view, Sandoz "seeks to transform the entire claim to cover an alleged 'pre-existing' bacteria issue that is not addressed in the patent." UTC Brief at 25. UTC argues that nothing in the specification or prosecution history suggests that bacteria must be present in the pharmaceutical preparation prior to the step of supplying the active agent with a buffer. UTC points out that the word "existing" – which Sandoz proposes be added to the claim – does not appear anywhere in the '007 specification, and is inconsistent with the specification's emphasis on addressing bacterial contamination that may occur during administration. UTC argues that Sandoz would limit claim 1 to contamination that may occur during manufacturing or any other step before the buffer is added or the pharmaceutical agent is diluted in a hospital or similar setting, even as the '007 specification makes clear that its methods are directed to microbes "that might be present, or become present, in the buffer solution" and as such are selective against "particularly troublesome classes of bacteria" (*i.e.*, gram negative bacteria) that are "commonplace in the hospital environments" in which such pharmaceutical agents may be diluted and administered. (*See* '007 patent at 4:9-14; 1:32-34 (emphasis added)). UTC also points out that the '007 specification further teaches that the benefits of the invention extend to medical devices that administer an active agent to patients after dilution in buffer solutions. (*See, e.g.*, *id.* at 1:38-40 ("Also, gram negative bacteria are associated with water contamination which can occur with chronic indwelling catheters such as used with intravenous administration.")).

Furthermore, in UTC's view, Sandoz's proposed construction of the disputed term would also mean that the meaning of "pharmaceutical preparation," a term that is not technically in

dispute at this time, would be distorted in a way that is inconsistent with how that term is used in the patent. That is, UTC argues that by limiting claim 1 to selectively killing and inhibiting bacteria "that are present in a pharmaceutical preparation prior to the step of supplying the active agent with a buffer," Sandoz's construction would require the claim term "pharmaceutical preparation" to refer to the active agent (i.e., treprostinil and treprostinil sodium) "prior to" the addition of a buffer. However, UTC argues that as used in the specification, the term "pharmaceutical preparation" clearly refers to the combination of an active agent with a buffer,[5] so a construction of the disputed term that would require a contrary meaning of "pharmaceutical preparation" must be improper.

Claim Construction

The Court agrees with UTC that Sandoz's construction would transform the entire claim to cover a "pre-existing" bacteria issue that is clearly not addressed in the patent. In addition, the Court disagrees with Sandoz insofar as Sandoz argues that the Court's role in claim construction is to resolve every possible alleged ambiguity in the claim terms. *See, e.g.*, Sandoz Br. at 25 (arguing against UTC's construction because it would "leave[] unresolved" certain questions). For the purposes of construing this term as well as several other disputed terms in this litigation, it is important to note that "a sound claim construction need not always purge every shred of

[5] UTC provides the following several examples. It says that the specification teaches that "[t]he present invention is directed to the use of buffer systems to maintain a specific pH range as anticidal agents in pharmaceutical preparations." ('007 patent at 3:54-56 (emphasis added)). Figures 6-15 also disclose the activity of "pharmaceutical preparations" that are the combination of an active agent (treprostinil) with a buffer solution. (*See, e.g.*, *id.* at 3:1-4 ("FIG. 7 is a graph showing the antimicrobial activity (CFU) over time (days) of various buffer systems against . . . a gram negative bacterium, in a pharmaceutical preparation comprising 0.004 mg/mL treprostinil.") (emphasis added); *see also id.* at 2:50-67, 3:6-15). Likewise, claim 9, which depends on claim 1, involves "injecting the pharmaceutical preparation into a mammal" – something that would only occur after the active agent is combined with a buffer. (*Id.* at 8:15-16 (emphasis added)).

ambiguity. The resolution of some line-drawing problems . . . is properly left to the trier of fact." *See Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 806 (Fed. Cir. 2007) (citing *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1355 (Fed. Cir. 1998) ("[A]fter the court has defined the claim with whatever specificity and precision is warranted by the language of the claim and the evidence bearing on the proper construction, the task of determining whether the construed claim reads on the accused product is for the finder of fact.").

Here, Sandoz wants the Court to hold that certain phrasing in the claim language requires that bacteria be present in the pharmaceutical preparation prior to the step of adding the buffer. The Court disagrees that "pre-existing" bacteria are required by the claim language. The '007 specification makes clear that its methods are directed to microbes "that might be present, or become present, in the buffer solution," so Sandoz's proposed construction is faulty. (*See, e.g.*, '007 patent at 4:9-14). Sandoz's construction is also at odds with the '007 specification's teaching that the benefits of the invention extend to medical devices that administer an active agent to a patients after their dilution in buffer solutions, (s*ee, e.g.*, *id.* at 1:38-40) and the specification's use of the term "pharmaceutical formulation."

In the Court's view, this term in claim 1 should be accorded its plain and ordinary meaning, consistent with the purpose of the invention to reduce the likelihood of occurrence of bloodstream infections due to bacterial contamination occurring during or after dilution, but prior to injection into the bloodstream. ('007 patent at 4:8-10; 1:38-40). The mere fact that the bacteria must be in the pharmaceutical preparation when they are killed does not mean that they have to be present before the active agent is diluted with a buffer. Sandoz's proposed construction – which essentially adds limitations to the claim – violates the fundamental claim

construction rule that "courts may not redraft claims." *See Becton Dickenson & Co. v. C.R. Bard, Inc.*, 922 F.2d 792, 800 (Fed. Cir. 1990).

The Court also notes that UTC's alternate construction – replacing the phrases "selectively killing" and "inhibiting the growth of" with "preferentially reducing" and "preventing the increase of", respectively – is neither necessary nor helpful. The words, standing on their own and in the context of the claims, are understandable to a POSITA (and even to a layperson). Accordingly, the Court rules that no construction of this disputed term is necessary, and it will be accorded its plain and ordinary meaning.

Term 3: "the method comprising supplying the active agent with a buffer comprising glycine and having a pH of greater than 10 with low buffer capacity" ('007 patent, claim 1)

The Court now turns to the second of the disputed terms in claim 1 – "the method comprising supplying the active agent with a buffer comprising glycine and having a pH of greater than 10 with low buffer capacity." The parties proposed constructions are:

UTC's Construction	Sandoz's Construction
Plain and ordinary meaning. To the extent the Court determines that this term requires construction, UTC proposes the following: "the method comprising supplying the active therapeutic agent (with or without one or more inactive ingredients, such as metacresol) with a buffer comprising glycine and having a pH of greater than 10 with low buffer capacity"	"The method includes the step of supplying the active agent with a buffer comprising glycine and having a pH of greater than 10 with low buffering capacity to selectively kill the existing gram negative bacteria and inhibit the growth of the existing gram positive bacteria"

Again, UTC argues that this term should be given its plain and ordinary meaning. Consistent with its argument regarding the previous Claim 1 term in dispute, Sandoz argues that UTC's approach is unclear because it leaves open the question of whether the bacteria to be

killed and inhibited exist in the pharmaceutical preparation prior to the method step. To resolve this purportedly "open question", Sandoz proposes adding "to selectively kill the existing gram negative bacteria and inhibit the growth of the existing gram positive bacteria," and replacing the word "comprising" with "includes the step of." UTC objects to these proposals on the same grounds that it objected to the previous disputed term from Claim 1: namely, because Sandoz's construction improperly adds limitations that are inconsistent with the purposes of the claimed invention as set forth in the specification.

UTC also alternatively proposes to interpret the term "active agent" as the "active therapeutic agent (with or without one or more inactive ingredients, such as metacresol)." UTC says that this will clarify that the "active agent" refers to the "active therapeutic agent" in the pharmaceutical preparation, and that, as UTC argues, the presence of a preservative such as metacresol or other inactive agents does not take a method outside of the scope of claim 1. UTC Br. at 24 (citing '007 patent at FIGS. 1-5).

Claim Construction

As with the previous term, the Court declines to assign a construction and will interpret this term according to its plain and ordinary meaning. Sandoz's proposed construction improperly adds a limitation to the claim that is inconsistent with the description of the invention as set forth in the specification. The Court again rejects UTC's alternative proposal, this time because, much like Sandoz's proposals, UTC's construction seems to improperly add language to the claims where it is unnecessary and without any basis. Indeed, the '007 patent does not even mention metacresol, but UTC asks this Court to clarify that it or other preservatives and inactive agents may be included in the term "active agent". Accordingly, this term and the entirety of Claim 1 will be accorded their plain and ordinary meanings.

Term 4: "Wherein the administration reduces the gram negative bacteria and inhibits the growth of gram positive bacteria" ('007 patent, claim 11)

The phrase "wherein the administration reduces the gram negative bacteria and inhibits the growth of gram positive bacteria" is found in claim 11 of the '007 patent. The parties' proposed constructions are:

UTC's Construction	Sandoz's Construction
Plain and ordinary meaning. To the extent the Court determines that this term requires construction, UTC proposes the following: "wherein the administration reduces the gram negative bacteria and prevents the increase of gram positive bacteria"	"wherein the administration reduces the gram negative bacteria and inhibits the growth of gram positive bacteria present in the blood stream"

Claim 11 reads in pertinent part:

> A method of reducing the occurrence of blood stream infections in a mammal being treated with an active agent comprising administering to the mammal the active agent with a buffer . . . and wherein the administration reduces the gram negative bacteria and inhibits the growth of gram positive bacteria.

('007 patent at 8:20-27). UTC's primary argument is that the term needs no construction, and its alternative proposal simply changes the words "inhibits the growth of" to "prevents the increase of." Reprising its arguments from claim 1, Sandoz says that UTC's proposed construction is unclear and ambiguous because it "leaves open the question of whether or not the bacteria to be reduced and inhibited already exist in the blood stream of a mammal prior to the administration step." Sandoz Br. at 37.

Sandoz's proposed construction adds the phrase "present in the blood stream" to the end of the disputed term. Sandoz argues that the plain language of the claim requires that the

bacteria are present in the blood stream of a mammal prior to administration of the buffer and active agent:

> Because the step of administering the buffer and active agent to the mammal is what kills and inhibits the growth of the bacteria, the bacteria must already be present in the mammal prior to administration. Further, because the object of the claimed method is a reduction in the incidence of *blood stream* infections, the bacteria to be reduced and inhibited must be in the blood stream.

Sandoz Br. at 34-35 (emphasis in original).

Sandoz further argues that its construction is supported both by the specification and the prosecution history. Sandoz claims that the prosecution history supports its construction in that during the course of the patent prosecution the patentees agreed to an Examiner's Amendment removing the language "prior to injection in the bloodstream" which had immediately followed the disputed term – "wherein the administration reduces the gram negative bacteria and inhibits the growth of gram positive bacteria" – from what is now claim 11, in order to obtain allowance of the claim. *See* Certification of Lauren N. Martin, Ex. 7 ("'007 Patent Prosecution History") at Sandoz-Trep0002795-97, 2803-9.

UTC argues that Sandoz's position "is nonsensical, at odds with the purpose of the invention, and a transparent attempt to introduce limitations not present in the claim to avoid Sandoz's plain infringement of this claim." UTC Brief at 29 (citing, *inter alia*, *Markman*, 517 U.S. at 390 (stating that claims are to be construed to "preserve the patent's internal coherence"); *Becton, Dickinson & Co. v. Tyco Healthcare Grp., LP*, 616 F.3d 1249, 1255 (Fed. Cir. 2010) ("[A] claim construction that renders asserted claims facially nonsensical cannot be correct."). According to UTC, Sandoz's position is belied by the claim itself and the specification as a whole in that Claim 11 and the '007 patent as are directed to a "method of *reducing the occurrence* of blood stream infections" from administration of the pharmaceutical product, and

not to treating already existing infections. UTC Br. at 30 (citing '007 patent at 2:11-19 (emphasis added); *id.* at 4:59-63.). According to UTC, the specification also makes clear that that its methods pertain to preventing bacterial contamination in medical devices and pharmaceutical preparations prior to and during administration – not to treatment in the blood stream. UTC Br. at 30-31 (citing '007 patent at 1:38-40 ("[G]ram negative bacteria are associated with water contamination which can occur with chronic indwelling catheters such as used with intravenous administration.")).

UTC also argues that despite Sandoz's argument, the prosecution history supports UTC's proposed construction. UTC argues that the removal of the limiting phrase "prior to injection into the blood stream" meant that the limitation was not necessary for patenting. UTC contends that adding this language back into the claim through claim construction would improperly restrict the claim term to the limitations removed by a broadening amendment. UTC Br. at 33 (citing *Transonic Sys., Inc. v. Non-Invasive Med. Techs. Corp.*, 143 F. App'x 320, 326 (Fed. Cir. 2005)).

Finally, and perhaps most fundamentally, UTC argues that through the combination of Sandoz's constructions of claims 1 and 11,[6] Sandoz would:

> exclude entirely from their scope the very methods that the '007 invention actually addresses: the reduction and inhibition of bacterial contaminants after the active agent is diluted in buffer, but before that pharmaceutical preparation is injected into the patient.

UTC Br. at 34. UTC argues that contrary to Sandoz's position, the patent claims, specification, and prosecution history make clear that the claims are not directed to treating mammals with

[6] Sandoz would narrow claim 1 to killing and inhibiting "existing" bacteria that are present in the pharmaceutical preparation prior to supplying the active agent with a buffer, and would narrow claim 11 to reducing and inhibiting the bacteria that are already present in the blood stream.

already-existing blood stream infections or to addressing bacteria present in a pharmaceutical formulation before dilution in a buffer.

Claim Construction

For the reasons stated by UTC, and for many of the same reasons stated in the Court's analysis regarding the disputed terms in Claim 1 of the '007 patent, the Court holds that the term does not need construction and should be accorded its plain and ordinary meaning. The term is sufficiently clear. Sandoz wants the Court to add language and limitations that seem to be inconsistent with the specification and the very purpose of the invention.

Term 5: "a pH between about 10 to about 12" (Claims 4, 16, and 24)

The final term the Court must construe – "a pH between about 10 to about 12" – is contained in Claims 4, 16, and 24 of the '007 patent. The parties' proposed constructions are:

UTC's Construction	Sandoz's Construction
Plain and ordinary meaning. To the extent the Court determines that this term requires construction, UTC proposes the following: "a pH between 10 and 12 with nominal and accepted variations recognizing the inherent inaccuracies in calculations and measurements"	"a pH of 10 to 12, including nominal and accepted variations above and below these values"

Citing Federal Circuit law, UTC argues that the term "about" can be given its ordinary meaning of "approximately". UTC Br. at 35-36 (citing, *inter alia*, *Merck*, 395 F.3d at 1367, 1369-70. UTC points to language in the specification, which UTC says provides additional explanation for why certain claims recite pH values of "about 10 to about 12." The specification states:

> The term "about" is used herein in recognition of the inherent inaccuracies in calculations and measurements in the art and to include nominal and accepted variations "about" the recited numeral.

('007 patent at 4:33-36.) According to UTC, this language confirms that the use of "about" is used in its plain and ordinary meaning – to indicate that certain measurements are "approximate." UTC argues that should the Court construe the term, it should apply UTC's construction, which it says encompasses the "definition" of "about" from the patent specification by including "nominal and accepted variations." UTC Br. at 37.

Sandoz, like UTC, proposes a construction – "a pH of 10 to 12, including nominal and accepted variations above and below these values" – that it says is consistent with the "definition" of the term "about" from the specification, as well as with Federal Circuit precedent holding that the ordinary meaning of the term is "approximately". Sandoz also argues that its proposed construction is supported by the prosecution history. In a June 17, 2010 office action, the Examiner rejected claims 1, 12, and 24 as indefinite under 35 U.S.C. § 112 because they included the limitations "greater than about" and "less than about." ('007 Patent Prosecution History at Sandoz-Trep0002677). In particular, the Examiner stated as follows:

> Either the limitation is 'greater than' or the limitation is 'about.' Greater than is a static point while about is a dynamic point. As a result the recitation of 'greater than about' – renders the claims vague and indefinite. A point cannot be simultaneously static and dynamic.

(*Id.* at Sandoz-Trep0002677). The Examiner made the same argument with respect to the "less than about" language. (*Id.*).

In a response dated September 8, 2010, the patentee amended the "greater than about 10" and "less than about 4.5" language in the independent claims to instead recite "greater than 10" or "less than 4.5." (*Id.* at Sandoz-Trep00002775-77). In explaining why the indefiniteness rejection should be withdrawn, the patentee stated as follows:

> Claims 1, 12 and 24 stand rejected as allegedly indefinite for reciting "greater than about." The claims have been amended to "greater than." Similarly, claims 1 and 12 stand rejected as allegedly indefinite for reciting "less than about." These claims have been amended to "less than."

(*Id.* at Sandoz-Trep0002722). In contrast to the issued independent claims 1, 11 and 22, dependent claims 4, 16 and 24 continued to include the limitation "between about 10 to about 12." Sandoz contends that if the patentee wanted to limit these claims to values greater than 10, or between 10 and 12, the patentee could have done that, but instead the patentee chose not to delete the word "about". Accordingly, Sandoz argues that because the patentee chose to define the endpoints of the claimed pH range in the dependant claims as dynamic points, the pH range in dependent claims 4, 16 and 24 includes "nominal and accepted variations" above and below 10 and 12. Sandoz Br. at 31-32.

As stated in its briefs, Sandoz's problem with UTC's construction is that it "leaves unclear the question of whether the claimed pH range would include the two end points and 'nominal and accepted variations' above and below the end points.'" But at oral argument, it became clear that Sandoz's chief concern is that UTC's construction leaves unclear whether the range would include nominal and accepted variations *below* 10.

Claim Construction

The Court finds that Sandoz's proposed construction will impermissibly deviate from the definition provided in the '007 specification, which the Court must adhere to. *See, e.g.*, *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1249 (Fed. Cir. 1998). While the Court agrees with both parties insofar as they argue that the '007 specification defines about in a manner consistent with the plain and ordinary meaning the Federal Circuit has adopted, *see* Defendant's Responsive Claim Construction Brief [D.E. 72] at 28, the Court does not agree with the construction proposed by Sandoz, nor does the Court agree with UTC that the term should be

accorded its plain and ordinary meaning without further construction. The Court does not seek to redefine the ordinary meaning of "about", but instead wishes to define it using the words of the '007 patent specification while recognizing that the definition is consistent with its ordinary meaning.

UTC's alternative proposed construction – "a pH between 10 and 12 with nominal and accepted variations recognizing the inherent inaccuracies in calculations and measurements" – replaces the word "about" with the language from the '007 patent specification's definition. ('007 patent at 4:34-10). By contrast, Sandoz's replacement of the word "between" with the word "of" is impermissible and without any basis. Sandoz's construction also adds the words "above and below these values", and fails to add any language reflecting the '007 specification's statement that "'about' is used herein in recognition of the inherent inaccuracies in calculations and measurements in the art." This deviance from the definition in the specification violates the Federal Circuit's claim construction guidance. *See, e.g.*, *Phillips,* 415 F.3d at 1316.

Finally, Sandoz's arguments regarding the prosecution history also do not justify their proposed construction. *See* Plaintiff's Responsive Claim Construction Brief [D.E. 70] at 31-32.

Accordingly, the Court adopts UTC's proposed construction of this disputed claim term.

ORDER

The Court having reviewed the parties' submissions and having held oral argument on the disputed terms; and for the reasons set forth in the above memorandum;

IT IS on this 25th day of June, 2013;

ORDERED that the disputed terms shall be constructed as follows:

Term 1 – "pulmonary hypertension" – is construed as:

> increased resistance to pulmonary blood flow resulting in greater pressure in the circulation for any particular flow, which is generally defined through observations of pressures above the normal range pertaining in the majority of people residing at the same altitude and engaged in similar activities, and which includes both primary and secondary pulmonary hypertension as ordinarily understood by clinicians.

Term 2 – "A method of selectively killing gram negative bacteria and inhibiting the growth of gram positive bacteria in a pharmaceutical preparation" – requires no construction.

Term 3 – "the method comprising supplying the active agent with a buffer comprising glycine and having a pH of greater than 10 with low buffer capacity" – requires no construction.

Term 4 – "wherein the administration reduces the gram negative bacteria and inhibits the growth of gram positive bacteria" – requires no construction.

Term 5 – "a pH between about 10 to about 12" – is construed as:

> a pH between 10 and 12 with nominal and accepted variations recognizing the inherent inaccuracies in calculations and measurements.

s/Peter G. Sheridan
PETER G. SHERIDAN, U.S.D.J.

June 25, 2013