IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION

Palmetto Pharmaceuticals LLC, Plaintiff, v. AstraZeneca Pharmaceuticals LP, Defendant.	Civil Action No. 2:11-807-SB **ORDER ADOPTING MASTER DORITY'S REPORT AND RECOMMENDATION**

Pursuant to Rule 53 of the Federal Rules of Civil Procedure, the Court entered an order, with the consent of the parties, appointing Julian W. Dority as Master to assist the Court with complex issues of claim construction. See Markman v. Westview Instruments, Inc., 517 U.S. 370 (1996). Following a Markman hearing on January 13, 2015,[1] Master Dority issued a report and recommendation on March 9, 2015, construing the terms at issue. (See Entry 411.) The parties filed timely objections to Master Dority's report in April, and in June they requested a hearing pursuant to Rule 53(f). The Court held a hearing on July 15, 2015, and for the reasons stated during the hearing and the reasons set forth herein, the Court adopts Master Dority's report in full.

BACKGROUND

As set forth in Master Dority's report, U.S. Patent No. 6,465,516 B1 ("the '516 Patent"), entitled "Method of Stimulating Nitric Oxide Synthase," was issued on October 15,

[1] The parties exchanged proposed terms for construction in May of 2014, and the following month the parties exchanged proposed claim constructions and supporting evidence. On July 21, 2014, the parties filed their opening claim construction briefs, and they filed responsive briefs on August 8, 2014. On October 27, 2014, the Court entered its order appointing Master Dority and scheduling the January 2015 Markman hearing.

2002. The '516 Patent is a continuation of patent application number 08/833,842, which was filed on April 10, 1977, and was issued on October 19, 1999, as U.S. Patent No. 5,968,983 ("the '983 Patent").

A request for Ex Parte Reexamination of the '516 Patent was filed on March 26, 2010, and an Ex Parte Reexamination Certificate was issued on April 5, 2011, as 6,465,516 C1 ("the Reexamined '516 Patent"). During reexamination, the United States Patent and Trademark Office found that original claims 1 and 3-6 of the '516 Patent were patentable (as amended) and that original claims 7-14 and new claims 15-20 were patentable; original claim 2 was cancelled. Reexamined '517 Patent col. 1 ll. 17-26.

Palmetto Pharmaceuticals LLC ("Palmetto") filed this patent infringement action on April 5, 2011, alleging that AstraZeneca Pharmaceuticals LP ("AstraZeneca") infringes the claims of Palmetto's Reexamined '516 patent (via direct infringement, induced infringement, and contributory infringement) by making, offering to sell, and selling an Hmg-CoA reductase inhibitor called CRESTOR® (rosuvastatin calcium). The following is a representative claim of the Reexamined '516 Patent, with the terms requiring construction presented in bold.

> 1. **A method for treating a nonyperlipidemic subject who would benefit from increased Nitric Oxide production in a tissue** comprising:
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> > administering to the **nonhyperlipidemic subject in need of such treatment** a Hmg-CoA reductase inhibitor in an **amount effective to increase Nitric Oxide production** in said tissue of the subject.

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Reexamined '516 Patent col. 1 l. 28-col. 2 l. 5.

STANDARDS OF REVIEW

I. Claim Construction

Claim construction is the process by which a court determines "the meaning and scope of the patent claims asserted to be infringed." Markman v. Westview Industruments, Inc., 52 F.3d 967, 976 (Fed. Cir. 1995). Claim construction is a matter of law, and a court must construe a patent's claims before determining whether a patent has been infringed. Id. at 979. When construing a patent's claims, words "are generally given their ordinary and customary meaning," and "the 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." Phillips v. AWH Corp., 415 F.3d 1303, 1313-14 (Fed. Cir. 2005). A court may consider three sources when ascertaining the meaning of claims: (1) the claims themselves; (2) the specification; and (3) the prosecution history. Markman, 52 F.3d at 979 (quoting Unique Concepts, Inc. v. Brown, 939 F.2d 1558, 1561 (Fed. Cir. 1991)). After considering the intrinsic evidence, the Court also may consider extrinsic evidence–"that evidence which is external to the patent and file history, such as expert testimony, inventor testimony, dictionaries, and technical treatises and articles." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1584 (Fed. Cir. 1996). However, reliance on extrinsic evidence is only proper "when the claim language remains genuinely ambiguous after consideration of the intrinsic evidence." Bell & Howell Document Mgmt. Prods. Co. v. A Itek Sys., 132 F.3d 701, 706 (Fed. Cir. 1997).

II. Rule 53 of the Federal Rules of Civil Procedure

As previously set forth, the Court entered an order pursuant to Rule 53, with the

consent of the parties, appointing Master Dority to assist with claim construction issues. Pursuant to Rule 53(f)(2), "[a] party may file objections to–or a motion to adopt or modify–the master's order, report, or recommendations." Fed. R. Civ. P. 53(f)(2). In considering a party's objections, Rule 53(f) provides that a court must decide de novo all objections to findings of fact and conclusions of law made or recommended by a master. Fed. R. Civ. P. 53(f)(3)-(4). In addition, a "court may set aside a master's ruling on a procedural matter only for an abuse of discretion." Fed. R. Civ. P. 53(f)(5).

DISCUSSION

As an initial matter, the parties do not object to Master Dority's proposed constructions of three terms, which are set forth below, and after consideration, the Court adopts the Master's construction of these terms:

Claim Term/Phrase	Master Dority's Construction
"benefit"	"a reduction of a clinical event or a reduction of the risk of a clinical event"
"Nitric Oxide [production]"	"nitric oxide produced from the constitutive form of Nitric Oxide synthase"
"nonhyperlipidemic"	"having measured lipid levels below the recommended level for consideration of cholesterol-lowering drug treatment"

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Next, however, the parties do object to the remainder of Master Dority's proposed constructions. Specifically, Palmetto objects to Master Dority's interpretation of the Federal Circuit's decision in Jansen v. Rexall Sundown, Inc., 342 F.3d 1329 (Fed. Cir. 2003), and the resulting construction of a "subject who would benefit from increased Nitric

Oxide production in a tissue" and "subject in need of such treatment." Next, AstraZeneca objects to Master Dority's construction of the following terms: (1) "amount effective"; (2) "administering . . . irrespective of the subject's cholesterol level"; (3) "method for treating" and [such] treatment"; and (4) "increase" and "increased." The Court will address each of the parties' objections in turn.

I. Palmetto's Objection

In his report, Master Dority construed the phrases "subject who would benefit from increased Nitric Oxide production in a tissue" and "subject in need of such treatment" to mean a "subject having a recognized need for increased Nitric Oxide production in a tissue," and to require the "method for treating a nonhyperlipidemic subject who would benefit from increased Nitric Oxide production in a tissue" to be conducted with the intentional purpose of "increasing Nitric Oxide production in said tissue of the subject." Palmetto objects to this construction and argues that it runs counter to the Federal Circuit's decision in Jansen as well as Judge Gergel's claim construction order in Charleston Med.Therapeutics, Inc. v. AstraZeneca Pharms. LP, Civil Action Nos. 2:13-2078 and 2:13-3438 (collectively "the MUSC cases").

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A. Is Master Dority's construction based on an erroneous interpretation of Jansen and/or is it at odds with Judge Gergel's claim construction in the MUSC cases?

As Master Dority remarked in his report, both parties agree that some level of "intent" is required when practicing the method of claim 1 of the Reexamined '516 Patent, but the parties disagree about the focus of such "intent." On one hand, Palmetto contends that "the person practicing the method must intend to treat a subject who is at

risk for cardiovascular disease conditions and adverse events." On the other hand, AstraZeneca contends that the treating medical professional must intend to treat a nonhyperlipidemic subject with the purpose of increasing nitric oxide production in the subject's tissue. As previously set forth, Master Dority agreed in large part with AstraZeneca[2] and determined that "the focus of the intent is to treat a nonhyperlipidemic subject to increase Nitric Oxide production in the tissue of the subject." (Entry 411 at 16.) Stated differently, Master Dority found that "the Hmg-CoA reductase inhibitor must be administered to a nonhyperlipidemic subject with a recognized need for an increase in Nitric Oxide production with the intent to increase Nitric Oxide production." (Id.)

In its objections, Palmetto first asserts that Master Dority's construction runs counter to the Federal Circuit's decision in Jansen. Palmetto asserts that Master Dority failed to take into account the key differences between this case and Jansen, namely, that Jansen involved an over-the-counter supplement whereas CRESTOR® is a prescription drug. Palmetto contends: "So while a requirement for a recognized need may be important in cases having facts like Jansen, where laypersons purchase over-the-counter drugs to treat themselves, such a requirement should not be read into claims in the 'quite different' context of a drug obtainable only via a physician's prescription–the very issuance of which evidences 'a diagnosis and a knowing need to use the product for the stated purpose.'" (Entry 415 at 5.)

#6

Palmetto next asserts that Judge Gergel applied Jansen correctly in the MUSC

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[2] Master Dority did not find support for AstraZeneca's assertion that the intent can only be recognized by a treating medical professional and did not read such limitation into the claim.

cases, and Palmetto objects to Master Dority's failure to consider Judge Gergel's construction in his report. Stated simply, Palmetto contends that Master Dority's construction–unlike Judge Gergel's construction–"encourages doctors to be willfully ignorant or 'forgetful' to AstraZeneca's benefit, and makes proving infringement far more expensive and time consuming, also to AstraZeneca's benefit." (Entry 415 at 2.) Palmetto also objects that Master Dority did not cite to any expert testimony in reaching his conclusion regarding the intent element of Jansen.

Finally, Palmetto contends that Master Dority's construction renders dependent claims 18-20 of its'516 patent internally contradictory because dependent claims 18-20 require that the subject be selected on the basis of having hypertension, whereas Master Dority's construction would require that the subject be selected based on a recognized need for increased nitric oxide production.

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After review, the Court finds all of Palmetto's objections unavailing. As Master Dority recognized in his report, Claim 1 of the Reexamined '516 patent is similar to the patent claim in Jansen.

Claim in Jansen	Claim 1 of Reexamined '516 Patent
"**A method of treating** or preventing macrocytic-megaloblastic anemia" by "administering" a combinaton of folic acid and vitamin B12 "**to a human in need thereof.**" Jansen, 342 F.3d at 1330 (emphasis added).	"**A method for treating** a nonyperlipidemic subject who would benefit from increased Nitric Oxide production" by administering a statin to "the nonhyperlipidemic subject **in need of such treatment**" . . . "in an **amount effective to increase Nitric Oxide production**" in the subject. Reexamined '516 Patent col. 1 l. 28-col. 2 l. 5 (emphasis added).

In Jansen, the Federal Circuit began its claim construction "as always, with the ordinary meaning of the claim language." 342 F.3d at 1332. The court determined that "the claim preamble sets forth the objective of the method, and the body of the claim directs that the method be performed on someone 'in need.'" Id. at 1333. The court continued:

> [T]he claims' recitation of a patient or human "in need" gives life and meaning to the preambles' statement of purpose. [ ] The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed.

Id. (internal citation omitted). Thus, the court in Jansen construed the claim to require "that the combination of folic acid and vitamin B12 must be administered to a human with a recognized need to treat or prevent macrocytic-megaloblastic anemia." Id. at 1334.

Here, the Court finds that the preamble sets forth the objective of the method–"treating a nonhyperlipidemic subject who would benefit from increased Nitric Oxide production"–while the body of the claim directs that the method be performed on a subject "in need thereof." It is natural for the Court to conclude that the alleged infringer's state of mind is relevant in construing "in need thereof." Accordingly, as in Jansen, the Court finds that the preamble does not merely set forth a potential or desired effect; rather, it states the intentional purpose for which the method must be performed. Thus, consistent with Jansen, the Court agrees with Master Dority that the statin must be administered to a nonhyplipidemic subject with a recognized need for increased Nitric Oxide production, and with the intentional purpose of "increasing Nitric Oxide production in said tissue of the subject."

Importantly, with regard to Palmetto's objection that Jansen involved an over-the-

counter supplement rather than a prescription drug like CRESTOR®, the Court first notes that Jansen has been applied to prescription drugs. See, e.g., Pfizer Inc. v. Teva Pharms. USA, Inc., 803 F. Supp. 2d 397, 408-09 (E.D. Va. 2011) (applying Jansen in the context of erectile dysfunction drug VIAGRA®); Wyeth v. Mylan Pharms., Inc., No. 07-91, 2009 WL 1457732, at *10 (N.D. W. Va. May 22, 2009) (applying Jansen to the antidepressant known as EFFEXOR®); Schering Corp. v. Glenmark Pharms. Inc., No. 07-1334, 2008 WL 4307189, at *8-9 (D.N.J. Sept. 16, 2008) (applying Jansen to the cholesterol-reducing drug ZETIA®). Moreover, the Court notes that in Jansen, the court did not consider the non-prescription nature of the supplement in its *claim construction analysis*; rather, it did so in its *infringement analysis*, a matter not before the Court at this time.

Ultimately, the Court finds support for its construction in the plain language of the claim and the intrinsic evidence, and the Court does not believe that the extrinsic evidence relied on by Palmetto, namely, the expert opinion of Dr. Hallett, overcomes the claim language and the intrinsic evidence. Here, the preamble defines a "subject" as someone "who would benefit from increased Nitric Oxide production," and the body of the claim goes one step further, providing for the administration of a statin to the "subject in need of such treatment" . . . in "an amount effective **to increase Nitric Oxide production**." Reexamined '516 Patent col. 1 l. 28-col. 2 l. 5 (emphasis added). In addition, the title of the patent is "Method of Stimulating Nitric Oxide Synthase," and the patent's specification describes increasing Nitric Oxide as an object of the invention in numerous places. See '516 Patent at 3:21–31, 3:34–37, 4:30–36, 4:60–5:1. The Court also notes that the reexamination history supports its construction. For example, the inventor of the patent,

Dr. Kaesemeyer, submitted a sworn declaration during the reexamination process stating that "a nonhyperlipidemic subject **can be selected for treatment to increase Nitric Oxide production**, . . ." (Entry 369-7 at 3 (emphasis added).) Moreover, Palmetto agreed during reexamination "that treating a subject to increase Nitric Oxide production necessarily means that the subject is selected for treatment," so that its proposed addition of "selected on the basis of a need for" increased nitric oxide would have been "redundant." (Entry 370-8 at 8.)

Next, to the extent Palmetto argues that Master Dority's (and this Court's) construction is at odds with Judge Gergel's construction in the MUSC cases, the Court disagrees. In the MUSC cases, the claim language provided "**a method of treating a nitric oxide or cytokine mediated disorder in a cell**" by administering a statin. (Entry 415-1 at 21 (emphasis added). Judge Gergel thus determined that the focus of the MUSC claims was whether doctors are treating *disorders* that are mediated by Nitric Oxide and not whether doctors recognize that those disorders are mediated by Nitric Oxide. Judge Gergel stated:

> Nothing in the plain language requires that the person practicing the invention *know* that the disorder she is treating is a nitric oxide mediated disorder or a cytokine mediated disorder. Holding that such knowledge is required also creates a perverse incentive for treating doctors to remain ignorant; a person skilled in the art could avoid infringement by remaining ignorant of the cellular biology underpinning a particular disorder. Therefore, the Court construes the preamble to require that "the person practicing the method must intend to treat a nitric oxide or cytokine mediated disorder in a cell but need not recognize that the disorder he or she is treating is a nitric oxide or cytokine mediated disorder."

(Entry 415-1 at 22 (emphasis in original).)

First, as a practical matter, the Court does not believe that Judge Gergel's claim

construction in the MUSC cases is particularly relevant, as the claim language in the MUSC cases is different from the claim language before this Court. Specifically, the claims in the MUSC cases were directed at treating specified disorders, and Judge Gergel required a specific intent to treat those disorders. Here, on the other hand, the claims are directed at treating individuals "in need of" increased nitric oxide production, and the Court finds that the proper construction of the claims requires the specific intent to treat that need. In other words, the claim language of the Reexamined '516 Patent does not refer to the treatment of any disorder; rather, it refers to the treatment of a subject "in need of" increased Nitric Oxide production. Thus, the Court finds that nothing in Judge Gergel's order contradicts the conclusion that the intent required by the claim must be consistent with the claim's recited purpose, which, here, is "to increase Nitric Oxide production in said tissue of the subject."

Finally, the Court does not agree with Palmetto that Master Dority's (and this Court's) construction is inconsistent with dependent claims 18-20 of the Reexamined '516 Patent. A dependent claim adds limitations to an independent claim, and claims 18-20, which add a requirement that a "subject is selected on a basis of having hypertension," is not inconsistent with the requirement of claim 1 that a subject also must have a recognized need for increased Nitric Oxide production.

Ultimately, although Palmetto agrees that the claims require some kind of intent by the person practicing the claimed method, it believes the intent is "to treat a subject who is at risk for cardiovascular disease conditions and adverse events." The Court does not believe that Palmetto's proposed construction is supported by the claim language or the intrinsic evidence. Instead, the Court finds that the claim language and patent

specification are clearly directed to the treatment of subjects who would benefit from increased Nitric Oxide production. Accordingly, the Court overrules Palmetto's objections and construes the preamble of reexamined claim 1 along with the phrase "a subject in need of such treatment" to mean "a subject having a recognized need for increased Nitric Oxide production in a tissue" and to require the "method for treating a nonhyperlipidemic subject who would benefit from increased Nitric Oxide production in a tissue" to be conducted with the intentional purpose of "increasing Nitric Oxide production in said tissue of the subject."

II. AstraZeneca's Objections

As set forth above, AstraZeneca objects to Master Dority's construction of the following terms: (1) "amount effective"; (2) "administering . . . irrespective of the subject's cholesterol level"; (3) "method for treating" and [such] treatment"; and (4) "increase" and "increased." Specifically, AstraZeneca contends that the language "amount effective to increase nitric oxide production" renders the patent at issue invalid as indefinite. Next, AstraZeneca contends that the deletion during reexamination of the claim limitation "administering . . . irrespective of the subject's cholesterol level" improperly broadened the claim. Third, AstraZeneca contends that "method for treating" and "[such] treatment" requires the administration of a combination of L-arginine and a statin rather than the administration of a statin alone. Lastly, AstraZeneca contends that Master Dority should not have given the terms "increase [Nitric Oxide production]" and "increased [Nitric Oxide production]" their plain and ordinary meaning but instead should have construed them to mean "increased by a mechanism of action independent of lowering a subject's cholesterol." The Court will consider each of these objections in turn.

#12

A. Is the term "amount effective" invalid as indefinite?

The Patent Act requires a patent specification to "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as [the] invention." 35 U.S.C. § 112. The Supreme Court has determined that a patent does not satisfy the statute's definiteness requirement and is, therefore, invalid "if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." Nautilus, Inc. v. Biosig Instruments, Inc., 134 S.Ct. 2120, 2124 (2014).

Here, Master Dority determined that the specification and prosecution history convey with reasonable certainty the amount of Hmg-CoA reductase inhibitor effective to increase Nitric Oxide production in the tissue of a subject. Thus, Master Dority did not find the phrase "amount effective" indefinite. Instead, Master Dority found that the phrase "amount effective" means "the dosage required to increase nitric oxide production."

AstraZeneca objects to Master Dority's finding and asserts that the term "amount effective" is indefinite because nitric oxide in a body cannot be reliably measured in a clinical setting, and therefore, it is unknown what does of a statin would be an "amount effective to increase nitric oxide production." Thus, according to AstraZeneca, a person of ordinary skill in the art would not understand this term with reasonable certainty.

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After consideration, the Court does not agree with AstraZeneca. As an initial matter, and as Master Dority noted, the law does not require that a person of ordinary skill in the art determine with 100 percent certainty the amount of Hmg-CoA reductase inhibitor effective to increase nitric oxide production. See Nautilus, 134 S.Ct. at 2129 ("The definiteness requirement, so understood, mandates clarity, while recognizing that absolute

precision is unattainable."). Rather, to be definite, the law requires that the claims, "read in light of the specification delineating the patent," inform "*with reasonable certainty*" those skilled in the art at the time the patent was filed. Id. (emphasis added). "One must bear in mind, moreover, that patents 'are not addressed to lawyers, or even to the public generally,' but rather to those skilled in the relevant art." Id. at 2128 (citing Carnegie Steel Co. v. Cambria Iron Co., 185 U.S. 403, 437 (1902)).

Here, the plain language of reexamined claim 1 provides "[a] method . . . comprising: administering to the nonhyperlipidemic subject . . . a Hmg-CoA reductase inhibitor in an amount effective to increase Nitric Oxide production in said tissue of the subject." Reexamined '516 Patent col.1 l. 28-col.2 l. 5. Because the plain language does not provide any dosage amounts, the Court considers this language in light of the specification and prosecution history. First, as Master Dority noted, the specification discloses certain dosing ratios of Hmg-CoA reductase inhibitor and L-arginine. See '516 Patent col. 6 ll. 9-16 and 35-42. While this dosage information refers to a *combination* of Hmg-CoA reductase inhibitor and L-arginine, the Court agrees with Master Dority that the prosecution history permits a person of ordinary skill in the art at the time of the invention to conclude with reasonable certainty the amount effective of Hmg-CoA reductase inhibitor–when administered alone–to increase nitric oxide production.

For example, during reexamination of the '516 patent, Dr. Wayne Kaesemeyer declared that "benefits will be observed in nonhyperlipidemic subjects receiving a statin at the FDA approved dosaging,[3] which is commensurate with the dosaging disclosed in

[3] Dr. Kaesemeyer listed the FDA approved dosaging for CRESTOR® as 5 to 40 mg once daily, and the FDA approved dosaging for LIPITOR® (an atorvastatin) as 10 to 80 mg

the '516 patent." (Entry 368-12 at 9, PALM 0012749.) Dr. Kaesemeyer also stated that "[d]osage selection for an individual subject is, of course, left to the physician's judgment." (Id.) Moreover, even the Examiner stated that "[t]he selection of an optimal mode of administration and an optimal dosing regimen are parameters well within the purview of those skilled in the art through no more than routine experimentation." (Entry 368-19 at 6, PALM0000581.) In fact, during prosecution of the '516 patent, the Examiner noted that "[t]he disclosed 'amount effective to increase endothelial cell nitric oxide synthase activity' in the specification overlaps with the therapeutic dosage range of pravastatin." (Entry 368-9 at 7, PALM0000674.) In addition, in describing the reasons for allowing the Reexamined '516 patent to issue, the Examiner noted that "[a] daily administration of 20 mg rosuvastatin, which is a standard dosage," resulted in certain benefits. (Entry 368-16 at 4.) Because the Court believes the intrinsic evidence permits a person of ordinary skill in the art at the time of the invention to conclude with reasonable certainty the dosage required to increase nitric oxide production, the Court does not find the term "amount effective" indefinite.[4]

B. Was claim 1 of the '516 Patent improperly broadened during reexamination?

#15

Pursuant to 35 U.S.C. § 305, entitled "conduct of reexamination proceedings," "[n]o

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once daily. (Entry 368-12 at 8-9.)

[4] The Court also notes that the extrinsic evidence supports its finding. For instance, Palmetto's expert, Dr. John Hallett, reported that "[v]arious statins and statin dosage information are discussed in the '516 patent . . . . These dosages are commensurate with standard dosages for treating patients who have hyperlipidemia." (Entry 368-10 at 6.) Dr. Hallett also stated in his reply report that "persons of ordinary skill in the art who prescribed statins were aware of the dosages that had been approved by the FDA, and would look to those dosages when treating a patient." (Entry 379-6 at 4.)

proposed amendment or new claim enlarging the scope of a claim of the patent will be permitted in a reexamination proceeding." "Whether amendments enlarge the scope of a claim is a matter of claim construction." In re Freeman, 30 F.3d 1459, 1464 (Fed. Cir. 1994). "The test for when a new claim enlarges the scope of an original claim under § 305 is the same as that under the two-year limitation for reissue applications adding enlarging claims under 35 U.S.C. § 251, last paragraph." Id. (citations omitted). The Federal Circuit has stated:

> a claim of a reissue application is broader in scope than the original claims if it contains within its scope any conceivable apparatus or process which would not have infringed the original patent . . . A claim that is broader in any respect is considered to be broader than the original claims even though it may be narrower in other respects.

Id. (citation omitted).

Here, AstraZeneca contends that the amendments entered during reexamination improperly broadened the scope of the claims of the '516 patent. Claim 1 of the '516 patent provided "[a] method for treating a subject who would benefit from increased Nitric Oxide production in a tissue comprising: administering to the subject in need of such treatment, *irrespective of the subject's cholesterol level*, a Hmg-CoA reductase inhibitor in an amount effective to increase Nitric Oxide production . . . ." '516 Patent col. 10 ll. 18-24 (emphasis added). The phrase "irrespective of the subject's cholesterol level" was removed during reexamination such that claim 1 of the Reexamined '516 Patent claims "[a] method for treating a *nonhyperlipidemic* subject . . . [by] administering to the *nonhyperlipidemic* subject." Reexamined '516 Patent col.1 ll. 28-col.2 l. 5 (emphasis added).

#16

AstraZeneca argues that the initial phrase "irrespective of the subject's cholesterol

level" should be construed to mean "administering . . . without the intent to alter the subject's cholesterol level." However, as Master Dority noted, the claim language makes no reference to "altering" or any "intent to alter" a subject's cholesterol, and, as such, AstraZeneca's construction, which seeks to import an element of intent where none existed, does not comport with the plain language of the claim. Furthermore, the Court agrees with Master Dority that the prosecution history clearly indicates that the Examiner understood the phrase "irrespective of the subject's cholesterol level" to encompass both hyperlipidemic and nonhyperlipidemic subjects. (See Entry 379-8 at 8, PALM 0012609 (stating that claims including phrase "irrespective of the subject's cholesterol level" "clearly encompass treating subjects who have hyperlipidemia and those that do not have hyperlipidemia").)

AstraZeneca next argues that because all people either have hyperlipidemia or do not have hyperlipidemia, Master Dority's construction renders the original claim term superfluous, which is impermissible. The Court does not agree. Moreover, the Court does not agree with AstraZeneca that the removal during reexamination of the phrase "irrespective of the subject's cholesterol level" improperly broadened the claim. Instead, the Court finds that the phrase's removal actually narrowed the patent; as the prosecution history indicates, the scope of claim 1 of the '516 patent included subjects without regard to whether they had hyperlipidemia or not, but during reexamination, the claim was amended to refer *only* to subjects classified as "nonhyperlipidemic." Thus, because claim 1 of the Reexamined '516 Patent is not broader in any respect from claim 1 of the original '516 Patent, the Court finds that claim 1 was not improperly broadened during reexamination.

#17

C. Do the terms "method for treating" and "[such] treatment" require administering a mixture or combination of L-arginine and a statin, rather than a statin alone?

In his report, Master Dority construed the terms "method for treating" and "[such] treatment" to require "the administration of a Hmg-CoA reductase inhibitor." (Entry 411 at 9-14.) In construing the terms, Master Dority considered the claim language, the specification, and the prosecution history. AstraZeneca objects to Master Dority's construction of the phrases and asserts that they require the administration of a *mixture* or *combination* of L-arginine and a Hmg-CoA reductase inhibitor. AstraZeneca contends that Master Dority's construction is broader than the invention described by the specification, as every embodiment of the invention described in the specification involves administering a mixture or combination of L-arginine and a statin rather than a statin alone.

As Master Dority noted, the plain language of claim 1 of the Reexamined '516 Patent simply refers to "administering . . . a Hmg-CoA reductase inhibitor" and does not require the "administration of a mixture or combination of L-arginine and Hmg-CoA reductase inhibitor," as asserted by AstraZeneca. Also, the prosecution history indicates that although the '516 Patent application *originally* required "administering a mixture of L-arginine and an inhibitor of Hmg-CoA reductase," the claim was deliberately amended to remove any reference to "a mixture of L-arginine." (See Entry 368-7 at 3, PALM0000010.) Moreover, the Examiner specifically acknowledged during prosecution that claim 1 did *not* require the administration of arginine. (See, e.g. Entry 268-9 at 6, PALM 0000673.)

#18

Despite the plain language of the claim and the prosecution history, AstraZeneca

contends that the terms should be construed to require the administration of a mixture or combination of L-arginine and a Hmg-CoA reductase inhibitor based on the specification language. However, as Master Dority noted: "particular embodiments appearing in the written description will not be used to limit claim language that has broader effect." Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc., 381 F.3d 1111, 1116 (Fed. Cir. 2004) (citations omitted). Thus, "even where a patent describes only a single embodiment, claims will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." Id. (quotation marks and citations omitted); see also Thorner v. Sony Computer Entertainment Am., LLC, 669 F.3d 1362, 1366-67 (Fed. Cir. 2012) ("It is likewise not enough that the only embodiments, or all of the embodiments, contain a particular limitation. We do not read limitations from the specification into claims; we do not redefine words. Only the patentee can do that. To constitute disclaimer, there must be a clear and unmistakable disclaimer."). Here, despite AstraZeneca's assertion that statements in the specification equate the term "invention" with the "administration of a mixture or combination of L-arginine and a Hmg-CoA reductase inhibitor," the Court agrees with Master Dority that nothing indicates a clear intention to limit the claim scope in such a way.

#19

In addition, as Master Dority noted, the extrinsic evidence indicates that any "mixture or combination" can be created by administering a Hmg-CoA reductase inhibitor, which then mixes or combines *in vivo* with L-arginine already present in the body. As Palmetto's expert, Dr. John Hallett, stated: "a physician would only need to write a prescription for the statin because arginine is already present in patients." (Entry 368-10

at 3.) Dr. Hallett also stated: "[i]t was well known to physicians in 1997 that arginine is both produced by the body and obtained from food, and thus is available for bio-transformation for the production of nitric oxide without the need for a special type of arginine supplementation." (Id.) In fact, even AstraZeneca's expert, Dr. David Harrison, stated that arginine is "certainly a hundred times higher" in the body, in particular in the endothelial cells, than the amount necessary, and that experiments have not shown a benefit from giving more arginine when there is already plenty present in the cell. (Entry 380-10 at 19.)

Based on the foregoing, the Court construes the phrases "method for treating" and "[such] treatment" in accordance with the plain language of the claim and the prosecution history to require "administering . . . a Hmg-CoA reductase inhibitor."

D. Do "increase" in Nitric Oxide production or "increased" Nitric Oxide production refer to an increase by a mechanism independent of lowering a subject's cholesterol level?

In his report, Master Dority determined that the terms "increase" and "increased" in claim 1 of the Reexamined '516 Patent relate to the "Nitric Oxide production," and that there was nothing inherently ambiguous about these terms as claimed. Thus, Master Dority found the following: "upon a review of the specification and the prosecution history, the plain and ordinary meaning of the terms 'increase' and 'increased' would be clear to a person of ordinary skill in the art at the time of the invention, and therefore, no construction is necessary." (Entry 411 at 24 (citations omitted).) In fact, Master Dority flatly rejected AstraZeneca's proposed construction as "unnecessary" and "unsupported by the intrinsic evidence." (Id.)

AstraZeneca objects to Master Dority's finding that the terms "increase" and

"increased" should be given their plain and ordinary meaning. Instead, AstraZeneca contends that the terms mean "increased by a mechanism of action independent of lowering a subject's cholesterol." AstraZeneca asserts: "It is inappropriate to adopt a term's plain and ordinary meaning when the specification clearly limits the broader scope that term might otherwise have." (Entry 416 at 25.)

After review, the Court disagrees with AstraZeneca. As Master Dority noted, the plain language of the claim does not require that any increase in a subject's nitric oxide production be "by a mechanism of action independent of lowering a subject's cholesterol level," and the Court declines to read such a limitation into the claim language. Moreover, the Court does not agree with AstraZeneca that the specification and prosecution history compel the Court to read such a limitation into the claim language. Instead, the Court agrees with Master Dority that there is nothing ambiguous about the terms "increase" and "increased," and the plain and ordinary meaning of those terms would be clear to a person of ordinary skill in the art at the time of the invention. Accordingly, the Court declines to adopt AstraZeneca's proposed construction and finds that no construction is necessary.

CONCLUSION

#21 After a de novo review of the matters objected to by the parties, the Court overrules Palmetto's objections (Entry 415) and AstraZeneca's objections (Entry 416), and the Court adopts Master Dority's R&R (Entry 411). Accordingly, the Court hereby construes the claim terms as follows:

Claim Term/Phrase	Construction
"benefit"	"a reduction of a clinical event or a reduction of the risk of a clinical event"
"Nitric Oxide [production]"	"nitric oxide produced from the constitutive form of Nitric Oxide synthase"
"nonhyperlipidemic"	"having measured lipid levels below the recommended level for consideration of cholesterol-lowering drug treatment"
"subject who would benefit from increased Nitric Oxide production in a tissue" and "subject in need of such treatment"	"subject having a recognized need for increased Nitric Oxide production in a tissue" and requires the "method for treating a nonhyperlipidemic subject who would benefit from increased Nitric Oxide production in a tissue" to be conducted with the intentional purpose of "increasing Nitric Oxide production in said tissue of the subject"
"amount effective"	"the dosage required to increase Nitric Oxide production in the tissue of the subject."
"method for treating" and "[such] treatment"	"administering a Hmg-CoA reductase inhibitor"
"increase" and "increased"	plain and ordinary meaning

AND IT IS SO ORDERED.

Sol Blatt, Jr.
Senior United States District Judge

November 30, 2015
Charleston, South Carolina