THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ABBOTT LABORATORIES and ABBOTT RESPIRATORY LLC,	:	
Plaintiffs,	:	
v.	:	Civ. No. 09-152-JJF-LPS
LUPIN LIMITED and LUPIN PHARMACEUTICALS, INC.,	:	
Defendants.	:	

REPORT AND RECOMMENDATION
REGARDING CLAIM CONSTRUCTION

Plaintiffs Abbott Laboratories and Abbott Respiratory LLC (collectively, "Abbott") filed this patent infringement action against Defendants Lupin Limited and Lupin Pharmaceuticals, Inc. (collectively, "Lupin") on March 6, 2009. (D.I. 1) Abbott alleges that Lupin infringes seven of its patents relating to Abbott's drug Niaspan®: U.S. Patent No. 6,080,428 (the "'428 patent"),[1] U.S. Patent No. 6,129,930 (the "'930 patent"),[2] U.S. Patent No. 7,011,848 (the "'848 patent"),[3] U.S. Patent No. 6,406,715 (the "'715 patent"),[4] U.S. Patent No. 6,818,229 (the "'229 patent"),[5] U.S. Patent No. 6,676,967 (the "'967 patent"),[6] and U.S. Patent No. 6,746,691 (the "'691

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[1]D.I. 62 is the parties' Joint Appendix. The '428 patent is found at JA000001-11.2 of the Joint Appendix. All subsequent citations to documents stamped "JA___" are references to the Joint Appendix.

[2]The '930 patent is found at D.I. 62, JA000012-28.

[3]The '848 patent is found at D.I. 62, JA000130-140.1.

[4]The '715 patent is found at D.I. 62, JA000029-49.4.

[5]The '229 patent is found at D.I. 62, JA000130-129.03.

[6]The '967 patent is found at D.I. 62, JA000050-75.02.

patent")[7] (collectively, the "Abbott patents"). The patents-in-suit are all part of the same family and all relate to compositions for and methods of treating hyperlipidemia. (D.I. 54 at 1; D.I. 55 at 3) Each of the Abbott patents refers to initial application 08/124,392, filed in 1993. (D.I. 54 at 2) That application was abandoned, but the continuation-in-part application 08/368,378, filed in 1995, issued in June 2000 as the '428 patent. (*Id.*) The '930 patent is a continuation-in-part from the '428 patent. (*Id.*) The '229, '691, '715, and '967 patents are all continuations-in-part from the '930 patent, and the '848 patent is a continuation from the '930 patent. (*Id.*) In this Report & Recommendation, I provide my recommendations as to the proper construction of the disputed claim terms in each of the Abbott patents.

BACKGROUND

A. Procedural Background

Claim construction issues in this case were referred to the undersigned magistrate judge per the Court's order of February 4, 2010. (D.I. 51) Briefing was completed in March 2010 (D.I. 54; D.I. 55; D.I. 58; D.I. 60) and a *Markman* hearing was held on May 21, 2010. *See* Transcript of May 21, 2010 hearing (D.I. 94) (hereinafter "Tr.").

B. Hyperlipidemia

Hyperlipidemia "is characterized by the presence of excess fats such as cholesterol and triglycerides in the blood stream," and is associated with abnormally high levels of "bad cholesterol," which includes high levels of low density lipoproteins ("LDL"), triglycerides, and apolipoprotein(a) ("Lp(a)"). (D.I. 55 at 3) Abnormally low levels of "good cholesterol," also

[7]The '691 patent is found at D.I. 62, JA000076-102.

known as high density lipoproteins ("HDL"), are also associated with hyperlipidemia. (*Id.*) Hyperlipidemia can lead to an increased risk of atherosclerosis, which is a hardening of the arteries due to an accumulation of cholesterol plaque in the arterial walls. (*Id.* at 3-4) Atherosclerosis may cause a number of significant health problems, such as coronary heart disease (that often leads to heart attacks), peripheral arterial disease, and strokes. (*Id.* at 4)

C. Prior Art Treatments for Hyperlipidemia

Niacin, or "nicotinic acid," has long been used to reduce total cholesterol, LDLs, triglycerides, and LP(a), while increasing HDLs. (*Id.*) Niacin administered to treat these conditions, however, is accompanied by uncomfortable and dangerous side effects. (*Id.*) The type of niacin treatment determines its effects and side effects; generally, niacin is given to patients in either immediate release or sustained release dosage forms. (D.I. 54 at 2-3)

"Immediate release" ("IR") niacin treatments are typically administered three or four times per day, and release nearly all of their niacin in the bloodstream very quickly (e.g., within 30 to 60 minutes of ingestion). (D.I. 55 at 4) While IR niacin treatments were generally known to reduce unfavorable cholesterol and increase desirable cholesterol, they were also commonly associated with "flushing," a side effect that causes a patient to develop a visibly red, uncomfortable, tingly and/or hot feeling for about one hour after each niacin dose. (*Id.*; D.I. 54 at 3) For some, these effects are severe enough to stop taking the drug. (D.I. 55 at 4) "As a result, physicians have been reluctant to recommend IR niacin (and patients have been reluctant to take it), despite its beneficial lipid-altering effects." (*Id.*)

"Sustained release" ("SR") niacin was developed to avoid the flushing side effect that accompanies IR niacin. (*Id.* at 5) Although normally dosed between two and four times per day,

SR niacin is designed to release niacin slowly into the bloodstream over a prolonged period of time – "usually 12 to 24 hours." (*Id.*) By lowering the peak concentration of niacin in the patient's blood at any one time, this dosage formulation reduces or eliminates the flushing effect. (*Id.*; D.I. 54 at 3) However, SR niacin has been shown to be less effective than IR niacin, yielding a significantly lower reduction in "bad" cholesterol and a much smaller increase in "good" cholesterol. (D.I. 55 at 5) Additionally, prior-art SR niacin therapies produced liver damage and harmful increases in uric acid or blood glucose levels. (*Id.*) Prior to Niaspan®, the FDA had not approved SR niacin for the treatment of hyperlipidemia. (*Id.* at 4)

The safety and usefulness of these various niacin treatments depend on the treatment's effects on a patient's liver. The Abbott patents discuss, among other things, three aspects of a patient's health that are tested to detect liver or other damage. (D.I. 54 at 3-4) Specifically, physicians monitor the risk of gout, diabetes, and liver damage in patients on drug therapies like niacin. (*Id.* at 4) The presence of high levels of uric acid in a patient's bloodstream is often correlated with gout (inflamation of the joints). (*Id.*) Excessive levels of glucose in the bloodstream can indicate diabetes. (*Id.*) When liver damage has occurred in a patient, three enzymes are released into the bloodstream: alanine transaminase (ALT), aspartate aminotransferase (AST), and alkaline phosphates (ALK). (*Id.*)

Some prior-art SR niacin products caused toxicity in the liver where the nicotinic acid (niacin) is broken down into its metabolites, an excess of which can cause liver damage. (D.I. 54 at 3) By contrast, IR niacin products cause less of a toxic effect because the liver generally breaks down heavy doses of niacin quickly, shielding the liver from dangerous metabolites, but the quicker release rate delivers less of the drug. (*Id.*)

D. The Patents-in-Suit

Given the harmful side effects of both IR and SR niacin, the Abbott patents claim a treatment regimen for niacin of one dose of an "effective antihyperlipidemic amount of a sustained release niacin composition, delivered once per day in the evening or at night." (D.I. 55 at 5-6 (citing '428 patent, col. 1 lines 12-21)) Dosing patients in the evening allowed the drug to act "when the rate of cholesterol synthesis was believed to be at its highest." (D.I. 55 at 6 (citing '715 patent, col. 4 line 54 to col. 5 line 55)) Further, dosing patients only once per day "helped prevent liver damage (hepatotoxicity) and increases in glucose and uric acid by avoiding constantly exposing the liver to nicotinic acid, as typically occurred when prior art [SR] products were administered several times per day." (D.I. 55 at 5 (citing '715 patent, col. 5 lines 17-26)) This basic dosing regimen was used to develop additional inventions "focused on the biopharmaceutical properties – such as the urinary metabolite profile, the plasma concentration profile, and the dissolution profile – necessary to effectively and safely treat hyperlipidemia." (D.I 55 at 6)

1. The '428 Patent

The '428 patent was filed on January 14, 1995 and issued on June 27, 2000, naming David Bova as the inventor. The disputed terms to be construed in the '428 patent appear in independent claim 1 and dependent claim 3 and are highlighted below:

> 1. A method of treating hyperlipidemia in a hyperlipidemic comprising dosing the hyperlipidemic with an effective antihyperlipidemic amount of nicotinic acid once per day in the evening or at night, wherein said nicotinic acid is combined with at least one pharmaceutically acceptable carrier to form ***an oral solid dosage form***.
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> * * *

3. A method as set forth in claim 1 which causes ***little or no serious liver damage***.

('428 patent, col. 12 lines 17-22, 26-27)

2. <u>The '930 Patent</u>

The '930 patent was filed on March 6, 1997 and issued on October 10, 2000 as a continuation-in-part of the '428 patent, naming David Bova as the inventor. The disputed terms to be construed in the '930 patent appear in independent claims 18, 51, 115, and 133. Claims 18, 51, and 115 are shown below as examples, with the disputed language emphasized:

18. A ***sustained release composition*** of nicotinic acid for oral administration to a patient once per day during the evening or night for providing an effective antihyperlipidemic amount of nicotinic acid to the patient to induce at least some lowering of total cholesterol, LDL cholesterol, triglycerides and Lp(a) and at least some increase in HDL cholesterol in the patient's blood stream, without causing abnormalities in uric acid levels or glucose levels or both to an extent which would require the use of said release composition by the patient to be discontinued, said sustained release composition comprising (a) an effective antihyperlipidemic amount of nicotinic acid, and (b) an excipient to provide sustained release of the nicotinic acid.

* * *

51. A daily method of treating hyperlipidemia in a patient without inducing treatment-limiting abnormalities in uric acid levels or glucose levels or both in the patient, said daily method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night as a single dose for providing an effective antihyperlipidemic amount of nicotinic acid to the patient to induce at least some decrease in levels of total cholesterol, LDL cholesterol, triglycerides and Lp(a) in the patient to induce at least some increase in levels of HDL cholesterol in the patient, without causing

abnormalities in either uric acid or glucose levels or both to an extent which would require said daily treatment to be discontinued by the patient, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an ***oral sustained release solid dosage form***.

* * *

115. A method of treating hyperlipidemia in a patient without inducing treatment-limiting (i) hepatotoxicity and (ii) abnormalities in uric acid levels or glucose levels or both, said method comprising orally dosing the patient with an effective antihyperlipidemic amount of nicotinic acid once per day during the evening or at night as a single dose, wherein the nicotinic acid is combined with at least one pharmaceutically acceptable component to form an oral sustained release solid dosage form, wherein the oral sustained release solid dosage form is effective in reducing a serum lipid without causing ***treatment-limiting (i) hepatotoxicity*** and **(ii)** ***elevations in uric acid levels or glucose levels or both in the patient to a level which would require said treatment to be discontinued by the patient*** when it is ingested by the patient once per day during the evening or at night as the single dose in accordance with said single dose treatment.

('930 patent, col. 16 lines 23-35, col. 18 lines 47-63, col. 24 lines 5-20)

3. The '229 Patent, '691 Patent, '715 Patent, and '967 Patent

The '229, '691, '715, and '967 patents (collectively, the "CIP patents") are continuation-in-part patents to the '930 patent. Many of the same disputed terms appear several times throughout these patents,[8] and representative examples are shown below:

17. An ***intermediate release nicotinic acid formulation***

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[8]Specifically, the disputed terms appear in: (i) claims 17 and 25 of the '229 patent; (ii) claim 13 of the '691 patent; (iii) claims 1, 3, 5, 7, 9, and 11 of the '715 patent; and (iv) claim 16 of the '967 patent.

suitable for oral administration once-a-day for treating hyperlipidemia without causing drug-induced hepatotoxicity to a level which would require use of said ***intermediate release nicotinic acid formulation*** to be discontinued, said ***intermediate release nicotinic acid formulation*** containing ***at least about 750 mg*** of nicotinic acid and having:

a nicotinuric acid Cmax in the range from between ***about 3 ug/ml*** and 3.2 ug/ml;

a nicotinuric acid Tmax in the range of between ***about 5.6 hours*** and ***about 6 hours***; and

an AUC for nicotinuric acid in the range of from between ***about 11 ughr/ml*** and ***about 13 ughr/ml***.

('229 patent, col. 30 lines 5-17)

1. An ***intermediate release nicotinic acid formulation*** suitable for oral administration once-a-day as a single dose for treating hyperlipidemia without causing drug-induced hepatotoxicity and (ii) elevations in uric acid or glucose or both, to levels which would require use of said ***intermediate release nicotinic acid formulation*** to be discontinued, said ***intermediate release nicotinic acid formulation*** comprising nicotinic acid and a swelling agent, said ***intermediate release nicotinic acid formulation*** having an in vitro urinary metabolic profile resulting from the absorption of the nicotinic acid released from the intermediate release formulation following the oral administration of the nicotinic acid formulation to an individual when the nicotinic acid formulation is dosed at ***about 1000 mg*** (a) nicotinic acid and nicotinic acid present in the urine in an amount of from ***about 4.0% to about 26%***, and (b) Pathway 2 metabolites present in the urine in an amount of from ***about 74% to about 95%***.

('715 patent, col. 28 line 54 to col. 29 line 4)

16. A method of reducing flushing in an individual being treated for a lipidemic disorder with an ***intermediate release nicotinic acid formulation*** suitable for oral administration once-a-day as a single dose without causing ***treatment-limiting hepatotoxicity*** and treatment-limiting elevations in uric acid or glucose levels or both ***in the individual to a level which would require use of the nicotinic acid formulation to be discontinued by the individual,*** comprising . . . .

a dissolution curve similarity fit factor F2 of at least ***about 44***, and

an in vitro dissolution profile, when measured in a type I dissolution apparatus (basket) according to U.S. Pharmacopeia XXII, at about 37° C. in deionized water at about 100 rpm, as follows

(a) less than ***about 15%*** of the nicotinic acid is released after about 1 hour in the apparatus,

(b) between ***about 15% and about 30%*** of the nicotinic acid is released after ***about 3 hours*** in the apparatus,

(c) between ***about 30% and about 45%*** of the nicotinic acid is released after ***about 6 hours*** in the apparatus,

(d) between **about 40% and about 60%** of the nicotinic acid is released after **about 9 hours** in the apparatus,

(e) between ***about 50% and about 75%*** of the nicotinic acid is released after ***about 12 hours*** in the apparatus, and

(f) at least ***about 75%*** of the nicotinic acid is released after about 20 hours in the apparatus.

('967 patent, col. 30 lines 22-62)

4. <u>The '848 Patent</u>

The '848 patent was filed on December 22, 1999 and issued on March 14, 2006, with

David Bova as the named inventor. The disputed terms in the '848 patent appear in claims 1 and 3 as follows:

> 1. A method of treating hyperlipidemia in a hyperlipidemic comprising ***dosing*** the hyperlipidemic with an effective antihyperlipidemic amount of nicotinic acid or compound metabolized to nicotinic acid by the body, once per day in the evening or at night combined with pharmaceutically acceptable carriers, to produce a reduction in total and LDL cholesterol, triglycerides and Lp(a), with a ***significant increase in HDL cholesterol.***
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> * * *
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> 3. A method of claim 1, which causes ***minimum liver damage, uric acid increases or elevations in fasting glucose levels***.

('848 patent, col. 15 line 66 to col. 16 lines 32-37, col. 16 lines 41-43)

LEGAL STANDARDS

"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) (internal quotation marks omitted). Construing the claims of a patent presents a question of law. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 977-78 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370, 388-90 (1996). "[T]here is no magic formula or catechism for conducting claim construction." *Phillips*, 415 F.3d at 1324. Instead, the court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.*

"[T]he words of a claim are generally given their ordinary and customary meaning . . . [which 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, i.e., as of the effective filing date of the patent application." *Id.* at 1312-13 (internal citations and quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted). The patent specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

While "the claims themselves provide substantial guidance as to the meaning of particular claim terms," the context of the surrounding words of the claim also must be considered. *Phillips*, 415 F.3d at 1314. Furthermore, "[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment . . . [b]ecause claim terms are normally used consistently throughout the patent . . . ." *Id.* (internal citation omitted).

It is likewise true that "[d]ifferences among claims can also be a useful guide . . . . 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 (internal citation omitted). This "presumption is especially strong when the limitation in dispute is the only meaningful difference between an independent and dependent claim, and one party is urging that the limitation in the dependent claim should be read into the independent claim." *SunRace Roots Enter. Co., v. SRAM Corp.*, 336 F.3d 1298, 1303 (Fed. Cir. 2003).

It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. It bears emphasis that "[e]ven when the specification describes only a single embodiment, the claims of the patent 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." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004) (internal quotation marks omitted), *aff'd*, 481 F.3d 1371 (Fed. Cir. 2007).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman*, 52 F.3d at 980. The prosecution history, which is "intrinsic evidence," "consists of the complete record of the proceedings before the PTO [Patent and Trademark Office] and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.*

A court also may rely on "extrinsic evidence," which "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. For instance, technical dictionaries can assist the court in determining the meaning of a term to those of skill in the relevant art because such dictionaries "endeavor to collect the accepted meanings of terms used in various fields of science and technology." *Phillips*, 415 F.3d at 1318. In addition, expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of ordinary skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.* Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [are] generated at the time of and for the

purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." *Id.* Overall, while extrinsic evidence "may be useful" to the court, it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19.

Finally, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998). It follows that "'a claim interpretation that would exclude the inventor's device is rarely the correct interpretation.'" *Osram GmbH v. Int'l Trade Comm'n*, 505 F.3d 1351, 1358 (Fed. Cir. 2007). Thus, if possible, claims should be construed to uphold validity. *See In re Yamamoto*, 740 F.2d 1569, 1571 (Fed. Cir. 1984).

CONSTRUCTION OF THE DISPUTED TERMS

The parties present over 50 disputed claim terms across the Abbott patents. Fortunately, however, the number of issues that must be resolved is far fewer. As is set out in detail below, the proper construction of the disputed terms follows from the answers to the following six questions: (A) do the Abbott patents exclude an "internal hydrophobic component"; (B) whether the "treatment-limiting" terms should be numerically defined; (C) whether "sustained release" can be defined in relation to "immediate release"; (D) whether "significant increase" should be numerically defined; (E) whether "intermediate release" can be defined in relation to both "sustained release" and "intermediate release"; and (F) whether "about" should be numerically defined.

A. Do the Abbott Patents Exclude an "Internal Hydrophobic Component"?[9]

The critical dispute between the parties over the construction of several claims of the Abbott patents is whether they should be construed to exclude "an internal hydrophobic component." (D.I. 55 at 2; D.I. 54 at 5-6) The parties agree that the resolution of this issue should apply to all the claims for which Lupin proposes this exclusionary language. (Tr. at 89-90) The disputed claims and the parties' proposed constructions for them are as follows:

Term/Phrase (Claim Nos.)	**Abbott's Proposed Construction**	**Lupin's Proposed Construction**
"Oral solid dosage form" ('428 patent, claim 1)	a drug product in a solid form to be administered by mouth	a drug product in a solid form to be administered by mouth a solid dosage form not containing an internal hydrophobic component designed for oral administration
"sustained release composition" ('930 patent, claims 18 & 133)	A composition which when administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release formulations	A composition not containing an internal hydrophobic component designed to release an active ingredient slower than an immediate release formulation

[9]The parties are in agreement that "hydrophobic" means "repelling, tending not to combine with, or incapable of dissolving in water." (D.I. 54 at 5 n.1)

Term/Phrase (Claim Nos.)	Abbott's Proposed Construction	Lupin's Proposed Construction
"oral sustained release solid dosage form" ('930 patent, claims 51 & 115)	A drug product sold in a solid form to be administered by mouth and which when so administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release formulations	A solid dosage form not containing an internal hydrophobic component designed for oral administration and designed to release an active ingredient slower than an immediate release formulation
"dosing" ('848 patent, claim 1)	administering a dose	administering a dosage form containing an active ingredient but not containing an internal hydrophobic component
"intermediate release nicotinic acid formulation" (''715 patent, claims 1, 3, 5, 7, 9, & 11) ('229 patent, claims 17 & 25) ('691 patent, claim 13) ('967 patent, claim 16)	A nicotinic acid formulation which, when administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release niacin formulations, but faster and different than other sustained release niacin formulations	A dosage form not containing an internal hydrophobic component that releases an active ingredient, namely, nicotinic acid, in vitro or in vivo over a period of time which is greater than 1 hour but less than 24 hours

i. <u>Abbott's Position</u>

Abbott argues that Lupin's proposed constructions excluding an "internal hydrophobic component" are facially incorrect. (D.I. 55 at 12) For instance, several of the '428 patent's dependent claims "expressly provide for tablets comprising a lubricating agent, such as stearic acid or magnesium stearate, which are hydrophobic components." (*Id.* (citing '428 patent, claims

8, 9)) Additionally, the '428 patent's specification describes the use of swelling agents, which "'include, but are not limited to, polymers such as . . . ethylcellulose and waxes . . . .'" (*Id.* at 13-14 (quoting '428 patent, col. 4 lines 14-18)) The specification also states that "[p]rocessing aids, such as lubricants, including stearic acid," may be used. ('428 patent, col. 4 lines 44-45) Ethylcellulose, waxes, and stearic acid are all hydrophobic components. (D.I. 55 at 14) Further, the specification provides that the swelling agent may be "'compounded with the nicotinic acid,' making it an 'internal' component of the tablet." (*Id.* (quoting '428 patent, col. 4 lines 5-12, col. 5 lines 12-13)) Abbott also notes that the '428 patent's specification does not exclude any particular component (hydrophobic or otherwise) from the invention; the only reference to a "hydrophobic component" in the patent is in the "Background of the Invention" section describing the prior art. (D.I. 55 at 13 & n.2 (citing '428 patent, col. 1 lines 62-65)) Therefore, Abbott concludes, the '428 patent explicitly encompasses an oral solid dosage form that contains an "internal hydrophobic component," so to construe claim 1 to exclude such a component would exclude one of the patent's preferred embodiments. (*Id.* at 13-14)

Regarding Lupin's argument that the '930 patent's specification excludes hydrophobic components by utilizing a "hydrophilic matrix controlled drug delivery system," Abbott responds that this description in the specification is merely "the best mode" for producing Niaspan®, which is only one embodiment of the '930 invention, and that nothing in the asserted claims *requires* use of a hydrophilic matrix delivery system. (D.I. 58 at 14) Moreover, Abbott contends that use of a hydrophilic matrix controlled delivery system does not preclude using hydrophobic components. (*Id.*) According to Abbott and its expert, Dr. McGinity, a person of ordinary skill in the art would understand that "hydrophobic components (e.g., ethylcellulose or waxes) may be

combined with the hydrophilic swelling agent to achieve the desired release of the active ingredient." (*Id.* (citing Supp. McGinity Decl. ¶ 18))

Abbott also argues that the prosecution history of the '428 patent's claim 1 undermines Lupin's proposed construction of "oral solid dosage form." According to Abbott, during "much" of the '428 patent's prosecution, the PTO Examiner took the position that the pending application and another patent, U.S. Patent No. 5,268,181 (the "O'Neill patent"), claimed the same invention, thereby requiring an interference to determine which inventor had priority of invention. (D.I. 55 at 15 (citing JA000270, '428 File History, June 10, 1996 Office Action and JA000292, '428 File History, Nov. 22, 1996 Office Communication)) The PTO applies a two-way test in order to decide whether the same invention is claimed by two patents: the claims of the application being examined "must anticipate or render obvious" the claims of the other patent and vice versa. *Eli Lilly & Co. v. Bd. of Regents of the Univ. of Wash.*, 334 F.3d 1264, 1268-69 (Fed. Cir. 2003).

The '428 patent inventor argued that no interference should be declared for two reasons: (1) the O'Neill patent was not anticipated by nor obvious in light of the '428 application because the O'Neill patent's claimed method "required a specific composition (that included an internal hydrophobic component), while the '428 application did not require such a specific composition;" and (2) the '428 application's claimed method centered around the dosing and time of administration, neither of which were anticipated by nor obvious in light of the O'Neill patent. (D.I. 55 at 16 (citing JA000277-78, '428 File History, Aug. 5, 1996 Amendment and Response at 3-4)) In concluding that an interference was not necessary, the Examiner appeared to accept the inventor's distinctions, stating that:

> [I]t is apparent that the composition employed in the methods of the ['428] applications are materially different than [the O'Neill patent], specifically there is no requirement of added hydrophobic component to be mixed with Niacin prior to tablet formulation.

(*Id.* at 16-17 (quoting JA000473, '428 File History, June 30, 1999 Notice of Allowability at 2)) In response, the '428 patent inventor confirmed that "'[u]nlike the [O'Neill patent], such unique methods, as claimed in claims 1-9 and 15-18 [of the '428 application], are accomplished . . . irrespective of whether a hydrophobic component is mixed with the nicotinic acid prior to tablet or other product formulation.'" (*Id.* at 17 (quoting JA000484-85, '428 File History, Oct. 15, 1999 Comments on Statement for Reasons for Allowance at 1-2))

With respect to the term "dosing" in claim 1 of the '848 patent, Abbott argues that its construction is confirmed by the term's plain language and the '848 patent's specification. (D.I. 55 at 36-37 (citing '848 patent, col. 3 lines 32-36, col. 9 lines 58-60)) Abbott also argues that the prosecution history confirms its construction. Original claim 1 of the '848 patent contained the term "dosing" and issued without amendment or argument between the Examiner and the applicant about the meaning of the term. (*Id.* at 37)

ii. Lupin's Position

Lupin asserts that both the specification and prosecution history of the '428 patent demonstrate that the disputed claims should be construed to include the negative limitation "not containing an internal hydrophobic component." (D.I. 54 at 6-7) Lupin maintains that the specification "identifies hydroxypropyl methylcelulose (a well-known hydrophilic material) as the preferred swelling agent" and discloses "no mechanism other than the use of a swelling agent

to obtain a sustained release."[10] (*Id.* at 7) Lupin further states that the Summary of the Invention portion of the '428 patent "no doubt identifies the formulation's essential components, *i.e.*, nicotinic acid and a hydrophilic material." (*Id.*)

In Lupin's view, the word "internal" means a "a hydrophobic component intimately mixed with niacin in the dosage form, e.g., intimately mixed with niacin in granules later compressed into tablets." (D.I. 60 at 2) The hydrophobic lubricating agents listed in the '428 patent are not "internal" to the niacin mixture, however. (*Id.* at 2) Rather, they are "external" components, "blended" with a granulated material (composed of niacin, the swelling agent Methocel, and the granulating/binding agent povidone) and then "pressed into tablets." (*Id.* at 2 (citing '930 patent, col. 7 lines 20-65 to col. 8 lines 25-32))[11] "The Methocel mixed with niacin to form the granules is called 'intragranular,' whereas the Methocel used with the lubricating agent is called 'extragranular.'" (*Id.* (citing '930 patent, col. 6 lines 1-18 (table IB), col. 6 lines 34-65)) Also, the lubricating agent is described as "external." (*Id.* (citing '930 patent, col. 5 lines 56-58); *see also* JA001118, '930 File History, Mar. 15, 1999 Office Action at 2)

Additionally, Lupin argues that the portion of the '930 specification describing the "'hydrophilic matrix controlled delivery system'" used to manufacture the preferred embodiment demonstrates that the patent excludes use of an internal hydrophobic component. (D.I. 54 at 8 (quoting '930 patent, col. 5 lines 20-36)) According to Lupin, to achieve the desired controlled-

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[10]"Hydrophilic" means "having an affinity for water; readily absorbing or dissolving in water." (D.I. 54 at 5 n.2)

[11]Lupin cites the '930 patent's specification in connection with the proper construction of the '428 patent, contending that "[t]o better understand the back and forth between the patentee and Examiner during prosecution of the '428 and '930 patents – and the resulting prosecution disclaimer – the Court should appreciate the significance of the word 'internal.'" (D.I. 60 at 2)

release delivery system as described in the '930 patent, the Abbott inventors used "polymer wetting, a phenomenon occurring with hydrophilic materials, not hydrophobic materials." (*Id.* at 8) Lupin insists that because "hydrophobic materials have little or no affinity for water, the desired 'wetting' and expansion in vivo would not occur with hydrophobic materials." (*Id.*) Thus, the '930 patent's repeated references to the word "hydrophilic" when discussing "the present invention" demonstrate that the claimed invention "concern[s] the use of hydrophilic materials together with nicotinic acid." (*Id.*)

With respect to the '428 patent's prosecution history, Lupin contends that because the Abbott patents constitute a family of patents stemming from a common patent application and containing common disclosures, "the claims must be interpreted consistently across all asserted patents." (*Id.* at 10) Further, "the prosecution histories of all the relatives in the family are relevant to the claim-construction analysis for a shared term or phrase, including the prosecution histories of later issued patents in the family." (*Id.* at 10-11 (citing *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1306-07 (Fed. Cir. 2007); *MBO Labs., Inc. v. Becton, Dickinson & Co.*, 474 F.3d 1323, 1327 (Fed. Cir. 2007))) Lupin acknowledges that the wording differs in the limitations among the various Abbott patents,[12] but insists that "they all concern the same concept, namely, an object containing nicotinic acid as an active ingredient intended for use

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[12]Lupin notes that the '428, '930, and CIP patents "include express formulation or dosage-form limitations, such as 'sustained release composition' and 'oral solid dosage form.'" (D.I. 54 at 14) The '848 patent, however, includes only "an implied limitation, i.e., the term 'dosing.'" (*Id.*) Claim 1 of the '848 patent recites the term "dosing" followed by requirements for an active ingredient (nicotinic acid) and inactive ingredients (pharmaceutically acceptable carriers), and, hence, "implicitly requires that 'dosing' occur with a dosage form containing active and inactive ingredients." (*Id.* (citing *Jamesbury Corp. v. United States*, 518 F.2d 1384, 1397-98 (Ct. Cl. 1975))

by individuals having hyperlipidemia. Consequently, the prosecution disclaimer attaching to any of these limitations should attach to all." (D.I. 54 at 14)

Specifically, in June 1995, the PTO Examiner rejected claims in the '428 patent application as "clearly anticipated" by the O'Neill patent. (*Id.* at 11 (citing JA000191, '428 File History, June 30, 1995 Office Action at 3)) The patentee responded that "the O'Neill patent claims are distinct at least because the O'Neill formulation requires a 'hydrophobic component'" and is based on prior art that "teach[es] that the hydrophobic component is an 'essential component of the invention,'" whereas the '428 patent inventor "did not find that 'a hydrophobic component' was essential for the efficacy of his nicotinic acid composition." (*Id.* at 11-12 (quoting JA000280-81, '428 File History, Aug. 5, 1996 Amendment and Response at 6-7)) Similarly, the '428 patentee explained during an October 1997 interview that the "'O'Neill patent requires 'hydrophobic component' where as in the instant claimed application there is no 'hydrophobic component.'" (*Id.* at 12 (quoting JA000351, '428 File History, Oct. 8, 1997 Interview Summary))

Thereafter, the patentee responded to the Examiner's final rejection by arguing that "'the specification of the . . . ['428 patent does not] teach or suggest the 'hydrophobic component' as claimed in independent claim 1 of the O'Neill patent.'" (*Id.* (quoting JA000397, '428 File History, Feb. 26, 1999 Response After Final at 9)) The Examiner was "apparently persuaded," and allowed the patent, stating that "the composition employed in the methods of the instant application are materially different than [the O'Neill patent], specifically there is no requirement of added hydrophobic component to be mixed with Niacin prior to tablet formulation." (*Id.* (quoting JA000473, '428 File History, June 30, 1999 Notice of Allowability at 2)) Thus,

according to Lupin, "during the '428 patent's prosecution, the patentee clearly and unequivocally disclaimed compositions or dosage forms that contain an internal hydrophobic component." (*Id.*)

Further, Lupin asserts that the '428 patentee repeated this "disclaimer" during prosecution of the continuation-in-part application that issued as the '930 patent. (*Id.* at 12-13) During an October 1998 interview with the Examiner, the Abbott patent inventor sought to overcome the PTO's rejection (based on the O'Neill patent) of some of the '930 patent's claims by agreeing to include the limitation that "'wherein said . . . [dosage form or tablet or preparation or composition] does not contain an internal hydrophobic component.'" (*Id.* at 13 (quoting JA00000957, '930 Patent File History, Oct. 28, 1998 Interview Summary)) The Examiner also noted that the prior art patents "have an internal hydrophobic component which is essential whereas in the instant ['930 patent] application there is no internal hydrophobic component . . . ." (*Id.* at 13 (quoting JA00000957, '930 Patent File History, Oct. 28, 1998 Interview Summary)) Additionally, Lupin argues that in a November 1998 amendment, the '930 patentee divided the pending claims into four groups and assigned the limitation "'wherein said . . . [dosage form or tablet or preparation or composition] does not contain an internal hydrophobic component'" to group I. (*Id.* (quoting JA00001009, '930 File History, Nov. 20, 1998 Amendment at 38)) While acknowledging that the '930 patentee chose to proceed with different claims, Lupin still contends that the proposed negative limitation "clearly disavowed nicotinic-acid compositions containing an internal hydrophobic component." (*Id.*)

Additionally, Lupin argues that the Abbott patent inventor's alleged disclaimer of formulations and dosage forms having an internal hydrophobic component in the patents issued after the '428 patent should be imputed to all the Abbott patents by virtue of their familial

relationship. (*Id.* at 14) Lupin's argument regarding the term "dosing" in claim 1 of the '848 patent, however, is unique to that term. Lupin asserts that although the '848 patent does not contain an express formulation or dosage-form limitation, it includes an implied limitation on the dosage form – *i.e.*, "dosing" in a dosage form containing an active ingredient ("nicotinic acid") and inactive ingredients ("pharmaceutically acceptable carriers"), but not containing an "internal hydrophobic component." (*Id.* at 14-15) Lupin also repeats its argument that the Abbott patents' prosecution histories support its proposed limitation of "no internal hydrophobic component." (*Id.*) In particular, Lupin contends that the fact that the '848 inventor changed the application's title from "Nicotinic Acid Compositions . . ." to "Hydrophobic Component Free Sustained Release Nicotinic Acid Compositions . . ." as part of a preliminary amendment shows that the patentee intended to limit the '848 patent dosage forms to those not containing an internal hydrophobic component. (D.I. 60 at 19-20) Although the patentee later changed the title back to its original form after the application was accepted, Lupin argues that its stated reason for doing so – that "[n]either the specification nor the claims contain the term 'hydrophobic'" – is meritless, because the specification recites "hydrophobic" when discussing the O'Neill patent's parent patent and contains the antonym "hydrophilic" to describe Niaspan®'s controlled-delivery system. (*Id.* at 20 (citing '848 patent, col. 2 lines 1-4, col. 5 lines 32-48))

iii. Recommended Construction

After reviewing the claims, specifications, and prosecution histories of the Abbott patents, as well as the extrinsic evidence of record, I am not persuaded that the disputed claim terms should include Lupin's proposed negative limitation "not containing an internal hydrophobic component." I recommend that the Court adopt Abbott's proposed constructions.

Among Lupin's strongest evidence for its proposed exclusion is the statement in the specification of the '428 patent – the "grandparent" patent – disclosing a hydrophilic substance as the preferred type of swelling agent. Specifically, as Lupin emphasizes, the '428 patent's specification states: "[a]n exemplary and preferred swelling agent is hydroxypropyl methylcellulose . . . ." ('428 patent, col. 4 lines 23-26) The force of this statement, however, is undermined by the following statement, which appears in the same portion of the '428 patent's specification:

> Such swelling agents include, but are not limited to, polymers such as sodium carboxymethylcellulose and ethylcellulose and waxes such as bees wax and natural materials such as gums and gelatins or mixtures of any of the above.

('428 patent, col. 4 lines 14-18) Ethylcellulose and waxes are hydrophobic components. (D.I. 56 AA Ex. B, McGinity Declaration ("McGinity Decl.") ¶ 44) Thus, the specification expressly contemplates use of hydrophobic components as swelling agents.

Lupin's proposal would inappropriately limit the '428 patent's invention to its preferred embodiment (*i.e.*, one containing hydrophilic, but not hydrophobic, components). The '428 patent's preferred embodiment is Niaspan®, which does not contain a hydrophobic material as a swelling agent.[13] "Even when the specification describes only a single embodiment, the claims

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[13]The parties vigorously dispute whether the lubricating agent – stearic acid, according to the '428 and '930 patents' preferred embodiments – is "internal" or "external" to the nicotinic acid granules that are eventually compressed into tablets. (D.I. 58 at 3; D.I. 60 at 3-4) However, there appears to be no dispute that the swelling agent is "internal" to the nicotinic granules. (*See* Tr. at 79; D.I. 55 at 14; D.I. 58 at 3; D.I. 60 at 2.) Lupin argues that because the only disclosed swelling agent in the Niaspan® preferred embodiment is a hydrophilic material, the Court should limit the claims' scope by excluding hydrophobic components. (Tr. at 66) Given that I am unconvinced that the Abbott patents should be limited to their preferred embodiment (*i.e.*, Niaspan®), there is no reason to limit the patents to the swelling agent used in Niaspan®. Hence, the specification's clear instruction that the swelling agent – which is an "internal"

of the patent 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." *Liebel-Flarsheim*, 358 F.3d at 906. Lupin has not pointed to words or expression of manifest exclusion or restriction in the '428 patent's specification that would justify reading the specification so restrictively.

Lupin's assertion that the Summary of the Invention discloses a formulation "containing *only* nicotinic acid and the hydrophilic swelling agent hydroxypropyl methylcellulose" (D.I. 54 at 7 (emphasis added)) is also incorrect. That passage states that the '428 invention "comprises" nicotinic acid and hydroxypropyl methylcellulose. ('428 patent, col. 3 lines 8-12) "Comprising is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir. 1997); *see also Mars, Inc. v. H.J. Heinz Co.*, 377 F.3d 1369, 1375-76 (Fed. Cir. 2004) (same); *Dow Chem. Co. v. Nova Chems. Corp. (Canada)*, 629 F. Supp. 2d 397, 407-08 (D. Del. 2009) (same). Another problem with Lupin's argument is that the Summary of the Invention is disclosing a preferred embodiment, but (as discussed above) there is no basis in the '428 patent to limit the scope of the claims to just this preferred embodiment.

For the reasons just explained in connection with the '428 patent, the '930 patent's specification also does not support including Lupin's proposed limitation of "no internal hydrophobic component." This conclusion is not altered by the '930 specification's description

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component, even according to Lupin – can include hydrophobic materials is persuasive evidence of the claims' scope.

of a "hydrophilic matrix controlled delivery system." Such a delivery system is an exemplary mode of manufacturing the preferred embodiment, but is itself only one way of practicing the '930 patent. ('930 patent, col. 4 line 65 to col. 5 line 37) Given that Lupin fails to direct the Court to support for Lupin's assertion that hydrophobic components could not be used in conjunction with a "hydrophilic matrix controlled delivery system," and that this kind of delivery system is not required by any of the asserted claims, I am not persuaded that the '930 patent should be construed to exclude hydrophobic components.

I turn now from the specifications to the prosecution histories. When the prosecution history of the '428 patent is considered as a whole, as it must be, *see Elbex Video, Ltd. v. Sensormatic Elecs. Corp.*, 508 F.3d 1366, 1372 (Fed. Cir. 2007), Lupin's contention that it contains a disclaimer (warranting inclusion of Lupin's proposed negative limitation) is revealed to be unpersuasive. A party seeking to show a prosecution disclaimer must demonstrate an "unambiguous" disclaimer, based on "clear and unmistakable evidence" that some of the scope that would otherwise be captured by the claim was relinquished during prosecution. *See Voda v. Cordis Corp.*, 536 F.3d 1311, 1321 (Fed. Cir. 2008). The same is true of disclaimers made during the prosecution history of a patent in the same family as the patent-in-suit. *See Verizon Servs. Corp.*, 503 F.3d at 1306-07.[14]

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[14]The parties cite what might be characterized as conflicting Federal Circuit precedents regarding whether, in order for a prosecution disclaimer to extend to related patents, the claim terms may use different language, as long as the related patents concern the same subject matter. *Compare, e.g.*, *RFID Tracker, Ltd. v. Wal-Mart Stores, Inc.*, 342 Fed. Appx. 628, 630 (Fed. Cir. 2009) ("Prosecution disclaimer may also arise from applicant's statements in a parent patent application if the parent application relates to the same subject matter as the claim language at issue.") *with Ventana Med. Sys. v. Biogenex Labs., Inc.*, 473 F.3d 1173, 1182 (Fed. Cir. 2006) (holding prosecution disclaimer does not generally extend to descendant patents using different claim language). It is not necessary to choose between the parties' competing interpretations of

Even when considering the prosecution histories of all of the Abbott patents,[15] I find no "unambiguous," "clear and unmistakable" disavowal of claim scope. A careful review of the file histories shows that the patentee consistently told the PTO only that his invention did not *require* a hydrophobic component; the patentee never stated that a hydrophobic component was *excluded* from the scope of the claims. Moreover, the patentee distinguished his invention from O'Neill by emphasizing that O'Neill required a specific composition, while the patents-in-suit do not, and further emphasizing that the patents-in-suit disclose a specific dosing size and timing, while the O'Neill patent does not. None of this constitutes the disavowal Lupin requires to prevail on its proposal to read the "internal hydrophobic" exclusion into the claims.

The analysis begins with the '428 patent. At first the Examiner rejected the '428 patent's claims as anticipated by the O'Neill patent. (D.I. 62, JA000270, '428 File History, June 10, 1996 Office Action) Then, however, the Examiner withdrew that rejection and indicated that an interference proceeding was necessary. (*Id.*) In response, the '428 inventor amended his claims and distinguished the O'Neill patent based on (1) the O'Neill patent's *requirement* of using a particular composition, whereas the '428 invention did not require a particular composition, and (2) the O'Neill patent's disclosure of administering the invention once per day, whereas the '428 patent requires its invention to be administered once daily *at a specific time of day*. (D.I. 62 JA000280, '428 File History, Aug. 5, 1996 Amendment and Response (hereinafter "August 1996

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the law on this point because, even considering the full prosecution histories of all of the patents-in-suit, there is no prosecution disclaimer.

[15]However, since the CIP patents have no prosecution histories, the available prosecution history documents concern only the '428 and '930 patents. (Tr. at 17)

Amendments") at 3-8)[16] Thus, the '428 inventor stated:

> The compositions described in new claim 15 [issued claim 10] and in the O'Neill patent claims are distinct at least because the O'Neill formulation ***requires*** a "hydrophobic component." . . . Significantly, [O'Neill's parent application] teach[es] that the hydrophobic component is an "essential component of the invention." . . . In contrast to [O'Neill's parent application], ***the ['428] inventor did not find that a "hydrophobic component" was essential for the efficacy*** of his nicotinic acid composition. Furthermore, the hydrophobic component is not included in the nicotinic acid composition of the ['428 invention], as defined by claim 15.

(D.I. 62, JA000280-281, August 1996 Amendments at 6-7) (emphasis added) While Lupin emphasizes the final sentence of this passage, the entirety of the passage demonstrates only that the hydrophobic component "required" by O'Neill and its parent application is not *required* by the '428 patent's then-pending claim 15. *See Elbex Video*, 508 F.3d at 1372 (finding no prosecution disclaimer, even though certain prosecution statements "could be argued to be a disclaimer," because, "[w]hen the prosecution history as a whole is considered, the inventor's response to the PTO is not as clear").

The same conclusion arises from review of the Examiner's October 7, 1997 Interview Summary. There, the Examiner stated that counsel for the '428 patent's applicant:

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[16]Abbott contends that the only relevant portions of the prosecution history of the August 1996 Amendments are the inventor's statements concerning pending claims 1-9, because only those claims are asserted in this litigation. (D.I. 58 at 6) Abbott insists that the inventor's statements regarding then-pending claim 15, which issued as claim 10 – which Abbott is not asserting against Lupin in this action – should not be considered. (D.I. 58 at 6) But the claim term in dispute – "oral solid dosage form" – also appears in issued claim 10. For at least that reason, the inventor's statements relating to claim 10 are relevant to construction of "oral solid dosage form" as that term is used in claim 1. *See Hormone Research Found. v. Genentech, Inc.*, 904 F.2d 1558, 1562 (Fed. Cir. 1990) ("Claim interpretation involves a review of the specification, the prosecution history, the claims (including unasserted as well as asserted claims), and, if necessary, other extrinsic evidence . . . .").

> explained that the O'Neill patent requires "hydrophobic component" where as in the ['428] application there is no "hydrophobic component." The examiner informed the counsel that claim 1 has the open-ended expression "comprising" and it is inclusive of all the unrecited ingredients. The counsel informed the examiner that claim 15 is different than claim 1 of the O'Neill patent as the claim 15 requires administering the niacin at night or evening which is not claimed by claim 1 of the O'Neill patent.

(D.I. 62, JA000351, '428 File History, Oct. 7, 1997 Interview Summary) This is not a clear disavowal of "hydrophobic components," internal or otherwise. The phrase "where as in the ['428] application there is no 'hydrophobic component'" refers to the "hydrophobic component" *required* by O'Neill. It is as natural to infer that counsel meant that the '428 application has no *required* "hydrophobic component" as it is to assume that counsel intended to disavow hydrophobic components completely. Thus, it is improper to conclude that the '428 patent's applicant intended to disavow an internal hydrophobic component. *See W.E. Haoll Co. v. Atlanta Corrugating, LLC*, 370 F.3d 1343, 1351-53 (Fed. Cir. 2004) (giving disputed terms their plain and ordinary meaning where Examiner's interview summary was susceptible to both limited reading and full ordinary meaning); *see also generally Univ. of Pittsburgh v. Hedrick*, 573 F.3d 1290, 1296-97 (Fed. Cir. 2009) (Examiner's interview summary too terse to inform definition of claim terms).

Lupin points to the '428 inventor's response to the Examiner's final rejection, in a section the inventor entitled "The Specification of the ['428 Application] Does Not Have Support for All Limitations Found in Independent Claim 1 in the O'Neill Patent." There the inventor stated:

> By way of example, the specification of the ['428 application] does not teach or suggest the particular hydroxypropyl methylcellulose claimed by independent claim 1 of the O'Neill Patent. Nor does the specification of the ['428 application] teach or suggest the "hydrophobic component" as claimed in independent claim 1 of

the O'Neill Patent.

(D.I. 62, JA000397, '428 File History, Feb. 26, 1999 Response After Final at 9) When viewing this February 26, 1999 Response as a whole, the '428 inventor repeatedly asserted that the key distinctions from the O'Neill patent are, *inter alia*, the '428 patent's lack of a specific nicotinic acid composition and the '428 patent's requirement of a particular time of day for dosing. (D.I. 62, JA000394-95, '428 File History, Feb. 26, 1999 Response After Final at 6-7) The excerpt relied on by Lupin, then, most reasonably shows that the '428 inventor was arguing that the O'Neill patent's claim 1 "***required*** both a particular hydroxypropyl methylcellulose (*i.e.*, '5-30% high viscosity hydroxypropyl methylcellulose having a nominal viscosity') and a particular quantity of hydrophobic component (*i.e.*, '2-20% of a hydrophobic component')." (August 1996 Amendments at 4 (quoting LA000962, O'Neill patent, col. 10 lines 24-25, 29-30)) (emphasis in original) By contrast, the '428 specification does not disclose a required, particular form of hydroxypropyl methylcellulose. Nor does it disclose the "'hydrophobic component' as claimed in independent claim 1 of the O'Neill Patent," because the hydrophobic component disclosed in O'Neill's claim 1 is an express limitation – and is thus "required" – as part of a particular formulation.

This conclusion is further supported by the Examiner's eventual decision to allow the '428 patent application over the potential interference by O'Neill. The Examiner's statement of reasons for allowance provides that:

> Upon reconsideration, reading the claims in light of the ['428 patent's] specification, it is apparent that the composition employed in the methods of instant application are materially different than [the O'Neill patent], ***specifically there is no requirement of added hydrophobic component to be mixed with Niacin prior to tablet formulation***.

(D.I. 62, JA000473, '428 File History, June 30, 1999 Notice of Allowability at 2) (emphasis added) Thus, the Notice of Allowability shows that the Examiner agreed with the inventor's argument that while the O'Neill patent "requires" an "added hydrophobic component to be mixed with Niacin prior to tablet formulation," the '428 patent does not. The inventor confirmed this distinction in his Comments on Reasons for Allowance, stating:

> Unlike [O'Neill], such unique methods, as claimed in claims 1-9 and 15-18, are accomplished . . . ***irrespective of whether a hydrophobic component is mixed with the nicotinic acid prior to tablet formulation. Thus, claims 1-9 and 15-18 are not limited to the requirement of adding a hydrophobic component for mixing with the nicotinic acid prior to tablet formulation***, as suggested by the Examiner in paragraph 1 of the Notice of Allowance.

(D.I. 62, JA000484-485, '428 File History, Oct. 15, 1999 Comments on Reasons for Allowance at 1-2) (emphasis added) In sum, the prosecution history of the '428 patent contains no unambiguous, clear, and unmistakable disavowal of "internal hydrophobic components."

Lupin's argument that a "repeated disclaimer" of "compositions or dosage forms that contain an internal hydrophobic component" is found in the prosecution history of the '930 patent is similarly unavailing. The inventor's March 3, 1998 amendments in response to the Examiner's rejection primarily address the inventor's attempt to distinguish the O'Neill patent on the grounds that the '930 patent accomplished its goals "without inducing hepatotoxicity" and without being limited to a particular nicotinic acid composition. (D.I. 62, JA000633, '930 File History, Mar. 3, 1998 Amendment at 27, 33-34) According to the Examiner's interview summary of October 1998, the Examiner and the applicants agreed that:

> [A]pplicants will amend all the independent claims and add claims from the parent case to include the limitation "wherein said (dosage form or tablet or preparation form) does not contain an internal hydrophobic component." The [O'Neill patent and its

> parent patent] have an internal hydrophobic component ***which is essential*** whereas in the instant application there is no internal hydrophobic component and external stearic acid is used only as lubricant.

(D.I. 62, JA000957, '930 File History, Oct. 28, 1998, Interview Summary) (emphasis added) Lupin urges that this statement demonstrates the '930 inventors' disclaimer of internal hydrophobic components. When read in the context of the entire prosecution history of the '930 patent, however, this statement (which is a statement of the Examiner, not the applicants) is not an unambiguous, clear, or unmistakable disclaimer.

After the interview summarized above, the '930 inventors submitted in November 1998 a group of claims ("Group I") that contained the agreed-upon limitation – "wherein said (dosage form or tablet or preparation form) does not contain an internal hydrophobic component." (D.I. 62, JA001028, '930 File History, Nov. 20, 1998 Amendment at 38) The inventor's second supplementary amendment of February 1999 sheds no further light on the Group I amendments. (D.I. 62, JA001104, '930 File History, Feb. 1, 1999 Second Supplemental Amendment at 10-12) After the Group I claims were rejected by the Examiner in March 1999 (D.I. 62, JA001119, '930 File History, Mar. 15, 1999 Office Action at 2), the inventor in December 1999 cancelled them without discussion (D.I. 62, JA001158, '930 File History, Dec. 3, 1999 Amendment After Final at 2). The '930 patent's remaining claims – those ***not*** including the limitation "no internal hydrophobic component" – were allowed soon thereafter. (D.I. 62, JA001161, '930 File History, Dec. 17, 1999 Notice of Allowability) The cancelled Group I claims, therefore, never issued.

The key here is that the inventors submitted claims that would have *excluded* a

hydrophobic component, but these claims were rejected. Thus, the claims as issued were not limited to the narrower scope proposed by the inventors. By implication, the claims that did issue – which do not contain the rejected narrowing limitation – are broader, indeed sufficiently broad to allow for *the possibility* of internal hydrophobic components. *See generally Schriber-Schroth Co. v. Cleveland Trust Co.*, 311 U.S. 211, 220-21 (1940) ("[A] claim in a patent as allowed must be read and interpreted with reference to claims that have been cancelled or rejected, and the claims allowed cannot by construction be read to cover what was thus eliminated from the patent."). Certainly, this is at least one reasonable interpretation of the prosecution history of the '930 patent. Therefore, again, these portions of the prosecution history do not provide the support Lupin requires to read into the claims the "internal hydrophobic component" exclusion Lupin proposes.[17]

In sum, therefore, even when considering the '930 patent's prosecution history in conjunction with the '428 patent's history, there is not sufficient evidence to support a finding a

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[17]Additionally, the November 1998 amendments predominantly concern the inventor's attempt to distinguish the '930 application from O'Neill based on the '930 patent's goal of treating hyperlipidemia "without inducing hepatotoxicity" and without being limited to a particular kind of nicotinic acid composition. (D.I. 62, JA001028, '930 File History, Nov. 28, 1998 Amendment at 57-58) With respect to the Group I negative limitation, the inventor explained that the '930 invention did not contain "any appreciable amount of an internal hydrophobic component, which functions in accordance with the specific and essential purpose defined for an internal hydrophobic component in the [O'Neill patent and its parent]." (*Id.* at 57) This explanation further underscores the impropriety of finding an express disclaimer. First, it appears to reserve the inclusion of "un-appreciable" amounts of an internal hydrophobic component. Second, it may also reserve use of internal hydrophobic components that do not "function[] in accordance with ***the specific and essential purpose defined for an internal hydrophobic component in the [O'Neill patent and its parent]***." (*Id.* (emphasis added))

prosecution disclaimer of "no internal hydrophobic component."[18] Thus, again, I recommend that the Court adopt Abbott's proposed construction of the multiple disputed claim terms in which Lupin would read in a limitation excluding an "internal hydrophobic component."

B. Treatment-limiting Terms

The "treatment-limiting terms" are a series of claim terms relating to various measures of liver enzymes, uric acid, and blood glucose levels that are referenced in various claims of the Abbott patents. For each of these terms, Abbott proposes to construe the limitation with reference to increases in these measurements that would require treatment with the claimed invention to be discontinued. By contrast, Lupin proposes specific, numerical levels of increases for each of these terms. The specific claim terms, and the parties' proposed constructions, are given in the table below.

Term/Phrase (Claim Nos.)	**Abbott's Proposed Construction**	**Lupin's Proposed Construction**
"little or no serious liver damage" ('428 patent, claim 3; '848 patent, claim 3)	No treatment-limiting hepatotoxicity that would require treatment to be discontinued by the patient	An increase in bloodstream liver enzyme levels, including aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase of no more than 9%

[18]The fact that the Abbott inventor changed the '848 patent's title during a preliminary amendment does not alter these conclusions.

Term/Phrase (Claim Nos.)	Abbott's Proposed Construction	Lupin's Proposed Construction
"minimum liver damage, uric acid increases, or elevations in fasting glucose levels" ('848 patent, claim 3)	No treatment-limiting hepatotoxicity or elevations in uric acid levels or glucose levels which would require treatment to be discontinued by the patient	An increase in the bloodstream liver enzyme levels, including aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase of no more than 9%, or repeated increases in bloodstream uric acid levels of no more than 8.4% or an increase in bloodstream fasting glucose levels of no more than 7.5%
"abnormalities in either uric acid or glucose levels or both to an extent which would require said daily treatment to be discontinued by the patient" ('930 patent, claim 51) **"treatment-limiting . . . elevations in uric acid levels or glucose levels or both in the patient to a level which would require said treatment to be discontinued by the patient"** ('930 patent, claim 115)	Repeated elevations in either uric acid levels, glucose levels or both to a level that is clinically significant and that requires discontinuation of current treatment	Repeated levels of either uric acid in the bloodstream beyond 7.5 mg/dl in women or 8.5 mg/dl in men or a level of glucose in the bloodstream beyond 115 mg/dl in women or 125 mg/dl in men
"treatment-limiting (i) hepatotoxicity . . . which would require said treatment to be discontinued by the patient" ('930 patent, claim 115)	Repeated elevations in liver enzymes (AST, ALT and/or alkaline phosphatase) to a level that is clinically significant and that requires discontinuation of current treatment	A bloodstream level beyond 150 mU/mL of aspartate aminotransferase, a level of beyond 165 mU/mL of alanine amineotransferase and/or a level beyond 420 mU/mL of alkaline phosphatase

Term/Phrase (Claim Nos.)	Abbott's Proposed Construction	Lupin's Proposed Construction
"treatment-limiting hepatotoxicity . . . in the individual to a level which would require use of the intermediate nicotinic acid formulation by the individual to be discontinued" ('967 patent, claim 16)	Repeated elevations in liver enzymes (AST, ALT and/or alkaline phosphate) to a level that is clinically significant and that requires discontinuation of current treatment	A bloodstream level beyond 150 mU/mL of aspartate aminotransferase, a level of beyond 165 mU/mL of alanine aminotransferase and/or a level beyond 420 mU/mL of alkaline phosphatase
"treatment-limiting elevations in uric acid or glucose levels or both in the individual to an level which would require use of the intermediate nicotinic acid formulation by the individual to be discontinued" ('967 patent, claim 16)	Repeated elevations in either uric acid levels, glucose levels or both to a level that is clinically significant and that requires discontinuation of current treatment	Repeated levels of either uric acid in the bloodstream beyond 7.5 mg/dl in women or 8.5 mg/dl in men or a level of glucose in the bloodstream beyond 115 mg/dl in women or 125 mg/dl in men

i. **Abbott's Position**

Abbott contends its proposed construction of the treatment-limiting terms is supported by the '428 patent's specification[19] and prosecution history. (D.I. 55 at 18-20, 40-41) The Background section of the patent, describing the invention and the problem it aimed to solve, refers to a study of a prior art SR niacin product given to 23 patients (hereinafter "the McKenney Study"), noting that "18 or 78 percent were forced to withdraw because liver function tests (LFTs) increased indicating potential liver damage." ('428 patent, col. 2 lines 19-32)[20] Thus, the

[19]"The portions of the '428 patent specification relating to the clinical testing of the invention are repeated in the '848 patent specification." (D.I. 58 at 31 n.14) Thus, this discussion of the '428 specification is also a discussion of the '848 specification.

[20]The McKenney Study can be found in the record at D.I. 61 at LA000887-92.

'428 invention aimed to "provide a method for employing a composition as above, for treating hyperlipidemia which results in little or no liver damage." (D.I. 55 at 19) The specification continues by adding "a group of 240 patients treated according to the present invention had zero patients drop out, based upon the same criteria for withdrawal" as used in the McKenney Study. ('428 patent, col. 11 lines 44-51) The specification concludes that the '428 invention "caused no elevation in liver function tests (*i.e.*, no liver damage)." ('428 patent, col. 11 lines 51-54) In Abbott's view, the specification thus establishes that "little or no serious liver damage" refers to the absence of "liver damage, that, in the view of the treating clinician, requires the patient to withdraw from treatment (*i.e.*, is 'treatment-limiting')." (D.I. 55 at 19)

Abbott argues that Lupin's proposed construction of the '428 patent's claim term "little or no serious liver damage," which imposes a cap of 9% on increases of particular liver enzymes, is inappropriate. The 9% figure is derived from Table IV in the specification, "which shows the results of tests for ALT levels in patients treated according to the invention of the '428 patent." (D.I. 55 at 19)[21] However, while 9% represents the mean change from baseline in patients' liver enzyme levels after four weeks, some patients who experienced even higher increases in those enzymes during the same time period were not withdrawn from treatment. (*Id.* (citing '428 patent, col. 11 lines 49-51 (Table IV))) Lupin's proposed construction would mean that about half of the patients in the study described in the specification suffered "serious liver damage" but continued treatment. (*Id.*) Thus, Lupin's construction "cannot be reconciled with the specifications' teaching that the invention 'caused no elevation in liver function tests (*i.e.*, no

[21]ALT, or alanine transaminase, is one of three liver enzymes physicians monitor in patients to detect liver damage or inflamation. (D.I. 54 at 4) The others are aspartate aminotranferase (AST) and alklaline phosphatase (ALK). (*Id.*)

liver damage).'" (D.I. 58 at 31 (quoting '428 patent, col. 11 lines 51-54)) The same is true for uric acid and glucose levels; approximately half the patients in the clinical trial had increases in uric acid and glucose levels over the "minimum," yet their treating physicians did not discontinue treatment. (*Id.*)

Abbott also argues that the '428 prosecution history supports its construction. Claim 3 of the '428 patent was allowed in its amended form, containing the limitation "little or no serious liver damage," without further amendment or argument during prosecution. Yet, the inventor described the '428 invention as a method of treatment that did not cause "'treatment-limiting side effects,'" such as hepatotoxicity. (D.I. 55 at 20 (quoting JA000392, '428 File History, Feb. 26, 1999 Response After Final Action at 4, and citing JA000484, '428 File History, Oct. 15, 1999 Comments on Statement for Reasons for Allowance at 1)) Abbott further asserts that nowhere in the prosecution history did the '428 inventor define or limit the disputed phrase to a particular upper numerical limit. By contrast, the invention was repeatedly characterized "as a treatment that did not cause treatment-limiting side effects such as liver damage." (*Id.*)

Additionally, Abbott's expert, Dr. Sacks, attests that a person ordinarily skilled in the art would agree that "little or no serious liver damage" should be interpreted according to Abbott's proposal. "A common threshold used by clinicians for assessing potential hepatotoxicity is if these liver enzymes exceed three times the upper limit of normal." (D.I. 56 AA Ex. C, Sacks Declaration (hereinafter "Sacks Decl.") ¶ 42) A patient's actual individual tolerable level of those liver enzymes, however, is determined by the patient's unique characteristics, "including factors such as the patient's starting level of liver enzymes before treatment, other medical conditions, and personal and family medical history." (*Id.*) This inherent variability can result in

one patient withdrawing from treatment due to only a doubling of liver enzyme levels, whereas another patient's enzyme levels could exceed three times the normal amount and yet not require withdrawal. (*Id.*) Consistent with this view, the Abbott patents' inventor, David Bova, in deposition testimony repeatedly rejected any assertion that there is a specific numerical threshold that constitutes "serious liver damage." (D.I. 58 at 32 n.16)

With respect to claims 15 and 115 of the '930 patent and claim 16 of the '967 patent, the parties' arguments supporting their respective proposals are very similar to the arguments just described (which relate to claim 3 of the '428 patent and claim 3 of the '848 patent). Essentially, Lupin wants to import the numerical limits disclosed in the Niaspan® clinical trial tables into the claim terms. Abbott argues that the specification does not support such importation, especially because a person ordinarily skilled in the art would understand that the meaning of "treatment-limiting" and "clinically significant" necessarily depends on the particular patient, physician, and laboratory involved.

Regarding these '930 and '967 claim terms, Abbott again emphasizes that Lupin's proposed "reference ranges" do not account for the fact that some patients were not withdrawn from the McKenney Study even though they experienced glucose levels that exceeded Lupin's proposed ranges. (D.I. 55 at 30) Abbott also observes that Lupin's construction does not employ the same methodology as the clinical trial tables to derive its proposed reference ranges; for liver enzymes, Lupin tripled the upper limits of the "reference ranges" but it did not do the same for the uric acid and glucose level "reference ranges." (D.I. 58 at 24) This variation, to Abbott, illustrates the arbitrary nature of Lupin's proposal.

In addition to repeatedly characterizing the '930 invention with reference to its lack of

treatment-limiting side effects, the '930 inventor stated to the PTO that a person ordinarily skilled in the art would know that, in the context of liver function tests, "normal" reference ranges for each individual patient are provided by the particular laboratory conducting the tests. (D.I. 55 at 31) Although "variations" in the normal reference ranges may occur, depending on how the particular testing laboratory validates its assay methodology, "normal and abnormal ranges for uric acid and glucose levels are well understood by those of skill in the art, regardless of which laboratory is selected to perform the assays." (*Id.* (quoting JA001061-62, '930 File History, Dec. 7, 1998 Transmittal Letter at 6-7)) Thus, another drawback to Lupin's proposals is that they attempt to read into the claims a set of "arbitrary, 'one-size-fits-all' numerical limitations," despite the fact that normal reference ranges vary by gender and age group. (*Id.*)

Further, Abbott's expert, Dr. Sacks, declares that a person of ordinary skill in the art would know that (1) niacin therapies necessitate regular testing of a patient's uric acid and glucose levels; (2) there is no single range of "normal" because the range varies from laboratory to laboratory; (3) if one test shows levels above "normal," second tests are commonly performed; and (4) even if later tests confirm an increase in levels, "the clinician will evaluate the results in the context of other factors, such as the patient's baseline levels, other medical conditions, and personal and family medical history." (Sacks Decl. ¶ 51)[22]

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[22]The parties do not agree as to the attributes of a person having ordinary skill in the art of the Abbott patents. Abbott proposes that such a person would hold a degree in either medicine or pharmacology. (D.I. 55 at 11) Lupin agrees that such individuals would be persons of skill in the art but also adds "formulators" who participate in the manufacture of drug products. (D.I. 60 at 39-40) Neither party believes that their difference of opinion on this point can or should be resolved in conjunction with claim construction. (Tr. at 46, 108; D.I. 60 at 40; *see also Sanofi-Aventis Deutscheland GmbH v. Glenmark Pharms. Inc.*, 2010 WL 715402, at *4 (D.N.J. Feb. 19, 2010)) Nor do I find it necessary to do so.

ii. Lupin's Position

Lupin argues that its proposed constructions, which add upper numerical limits to the claims, are necessary to give definition to the various claims, starting with claim 3 of the '428 patent and claim 3 of the '848 patent. (D.I. 54 at 42, 27) Lupin notes that several of the Abbott patents discuss uric acid levels (related to gout), glucose levels (related to diabetes), or hepatotoxicity (related to liver damage). (*Id.* at 3) Three liver enzymes (ALT, AST, and ALK) are tested to discover if liver inflammation or damage is present, and, according to Lupin, the liver toxicity measures for each enzyme generally do not differ by gender. (*Id.* at 4 (citing '428 patent, cols. 7-9); *id.* at 24 (citing '848 patent, col. 9 lines 61-67 to cols. 10-12)) Acceptable ranges for uric acid and glucose levels do differ by gender, however, with the normal range somewhat higher for men than for women. (*Id.* at 4 (citing '428 patent, cols. 9-10))

Tables III-V in the '428 and '848 patent specifications contain data from Niaspan® clinical trials demonstrating the product's improved safety over prior art products. (*Id.* at 24) The patents' specifications also state that liver damage is not occurring in a patient if there is no elevation in liver function tests. (*Id.* (citing '848 patent, col. 15 lines 40-42)) Although Table VIII shows a study in which there was no elevation in liver function tests, Tables III-V show elevations for patients taking Niaspan® of up to 6.6% for AST, up to 9% for ALT, and up to .005% for ALK. (*Id.* (citing '848 patent, cols. 10-12, col. 15 lines 40-42)) Thus, to Lupin, because the presence of any one of these enzymes "equates to potential liver damage," the claim terms "minimum damage" and "little or no serious liver damage" should be construed to mean "no more than a 9% increase from baseline levels." (*Id.* at 25) Likewise, Lupin proposes that "minimum . . . uric acid increases or elevations in fasting glucose levels" should be understood

as not exceeding 8.4% for uric acid and 7.5% for glucose, because those were the higher-end results reported for certain patients. (*Id.* (citing '848 patent, cols. 12-14))

Lupin argues that the doctrine of claim differentiation also supports its proposals. For instance, Abbott wants to construe the "minimum" and "little or no serious" phrases in the '428 and '848 patents in the same way it construes the phrases "treatment-limiting hepatotoxicity" and "treatment-limiting elevations" in claims 51 and 115 of the '930 patent: so that they all include the "requires discontinuation of current treatment" limitation.[23] (*Id.*) Lupin, however, insists that "minimum" cannot mean "treatment-limiting," because the primary dictionary definition of "minimum" is "the least possible amount, number or degree." (*Id.* (quoting D.I. 61, LA000019, *New Webster's Dictionary* (1993) at 6)) Thus, in contrast to "treatment-limiting," "minimum" should refer to a "toxicity tolerable to the patient yet insufficient to warrant discontinuation of treatment." (*Id.*) Additionally, the Abbott inventor, David Bova, included the phrase "minimum" in the '848 patent (which is a continuation of the '930 patent, itself the child of the '428 patent), whereas he had used "treatment-limiting" in the '930 patent. In Lupin's view, claim differentiation demands that these different claim terms appearing in related patents be given different meanings. (*Id.* (citing *Kara Tech., Inc. v. Stamps.com, Inc.*, 582 F.3d 1341, 1347 (Fed. Cir. 2009)))

Lupin further contends that David Bova testified that "little liver damage" referred to "elevations in the liver function tests" and that Tables III-V of the '428 patent reflect those elevations. (D.I. 54 at 27) Because the maximum elevation of the ALT enzyme was 9%, and the

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[23]As will be discussed, Abbott's proposed constructions of these '930 patent terms are, essentially, "repeated elevations in [the three liver enzymes] to a level that is clinically significant and that requires discontinuation of current treatment." (D.I. 55 at 28, 32)

presence of any one of the three liver enzymes indicates potential liver damage, "the 'little or no serious liver damage' tolerated by the patient should be a 9% increase from baseline." (*Id.*)

Lupin asserts that the declaration of Dr. Sacks, Abbott's expert – which argues that the threshold for determining liver damage in any one patient is based on a number of factors – fails to explain how ordinarily skilled artisans *other than doctors* could determine whether liver damage met or exceeded the "minimum" level, according to claim 3 of the '848 patent. (D.I. 60 at 29-30) Additionally, with respect to the term "minimum . . . uric acid increases, or elevations in fasting glucose levels," Lupin maintains that absent the "objective standards" supplied by its proposal (as derived from Tables VI-VII in the '848 patent), a doctor may "repeatedly test a patient and evaluate the test results based on personal experience and training." (*Id.* at 30) To Lupin, it follows that Abbott's proposed construction would not allow a portion of the ordinarily skilled artisans, specifically formulators and pharmacists, to know when a "minimum" elevation in uric acid or fasting glucose levels is reached. (*Id.*)

Similarly, Lupin faults Abbott's reliance on the McKenney Study, because Abbott's conclusion – that "'little or no serious liver damage' equates to 'no treatment-limiting hepatotoxicity'" – is one which would "require[] a doctor's judgment to discern." (*Id.*) In Lupin's view, the McKenney Study used *objective criteria* for patient withdrawal based on liver toxicity, specifically, when patients' liver function tests "were greater than three times the upper limit of normal." (*Id.* at 31) (internal quotation and citation omitted) Twelve of eighteen patients were withdrawn from the study based on that criteria; "with only 6 patients was there some degree of [subjective] clinical judgment," and even then the clinical judgment "applied to nonspecific symptoms not necessarily addressed by the asserted patent claims." (*Id.* (citing

LA000891, Table III (noting that withdrawn patients experienced rashes, diarrhea, and fatigue)))

Lupin's proposed construction with respect to "treatment-limiting" levels of uric acid and glucose levels is, again, derived from the '930 specification's tables showing the results of Niaspan® clinical trials. (D.I. 60 at 21-22) Lupin's proposal to triple the "reference ranges" for liver enzymes, however, is drawn from inventor David Bova's deposition and from Dr. Sacks' declaration. (*Id.* at 22) In Lupin's view, Bova testified that patients in Niaspan® clinical trials were discontinued when any liver enzyme reached three times the upper limit of normal according to FDA guidance. (*Id.* (citing D.I. 61, LA000433, Bova Dep. at 113)) Dr. Sacks declares that "a patient may have liver enzymes lower than three times [the upper limit of normal] and yet have symptoms indicative of hepatotoxicity that may warrant discontinuation of niacin treatment." (Sacks Decl.¶ 43) Lupin argues that its proposal is not strict in any sense; instead its construction incorporates "liver enzyme, glucose, and uric acid levels well above the results disclosed in the specifications for subjects taking Niaspan®." (D.I. 60 at 23; D.I. 54 at 19 & n.4)

Lupin also contends that during the '930 patent's prosecution, the '930 patent inventor undermined his position that "treatment-limiting" must be determined by physicians, when he stated:

> [T]he terms "treatment-limiting," "treatment-limiting elevations," or "treatment-limiting abnormalities," as used throughout the claims, . . . mean or refer to that level or range which is not or would not be acceptable to the [FDA]. This definition is supported by the specification at, for example, on page 17, lines 25-26, pages 18-28 and page 29, lines 6-9 and 13-14.

(D.I. 60 at 25 (quoting JA000855-56, '930 File History, Aug. 28, 1998 Amendment After Final

at 15-16)) As Lupin observes, here the inventor was citing to portions of the specification that include the clinical trial Tables III-VIII. (*Id.* (citing JA000536-48))

Finally, Lupin argues that Abbott's proposal to import the term "clinically significant" into the claims finds no support in the specification and is itself ambiguous. (D.I. 54 at 19-20) Also, Lupin notes that what is "clinically significant" will vary by laboratory, patient, or treating physician, rendering it too subjective a criterion to use as a measure. (*Id.* at 20)

iii. Recommended Construction

I recommend that the Court adopt Abbott's proposed constructions of these disputed terms. Abbott's proposals comport with both the specifications and prosecution histories of the '428 and '848 patents. The '428 and '848 specifications repeatedly characterize the invention by its lack of treatment-limiting side effects, in contrast to studies (such as the McKenney Study) in which a majority of patients were withdrawn due to such side effects. Similarly, the Abbott patents' inventor stated several times during prosecution that the invention did not cause "treatment-limiting" side effects, including hepatotoxicity. (D.I. 62, JA000392, '428 File History, Feb. 26, 1999 Response After Final at 4; D.I. 62, JA000484, '428 File History, Oct. 15, 1999, Comments on Statement for Reasons of Allowance at 1)

Both parties agree that what constitutes "treatment-limiting" (or causes discontinuation of treatment) for a particular patient necessarily turns on the judgment of the patient's individual treating physician. The dispute, then, is whether a physician's subjective discernment of a "normal" level of liver enzymes for a particular patient may permissibly be part of a claim's construction. The Federal Circuit has held that the use of functional claim terms (such as "enhancing amount" or "effective amount") are not indefinite, provided one of ordinary skill in

the art could determine the bounds of the claims without undue experimentation. *See Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1383-84 (Fed. Cir. 2003) ("'[E]ffective amount' is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without undue experimentation."); *Moore U.S.A., Inc. v. Standard Register Co.*, 229 F.3d 1091, 1111 (Fed. Cir. 2000) ("There is nothing wrong with defining the dimensions of a device in terms of the environment in which it is to be used."); *accord Tristrata Tech., Inc. v. ICN Pharms., Inc.*, 313 F. Supp. 2d 405, 410-11 (D. Del. 2004) ("[T]he Federal Circuit has held that the use of functional claim terms such as 'enhancing amount' or 'effective amount' are not indefinite, provided one of ordinary skill in the art could determine the bounds of the claims without undue experimentation."). "Treatment-limiting" and "require treatment to be discontinued" are, in the context of the patents-in-suit, such functional claim terms, and there is no persuasive reason to infer that a person having ordinary skill in the art would not be able to understand and follow them.[24]

Lupin's argument that claim differentiation precludes interpreting the terms "minimum

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[24]As has already been noted, the parties do not agree as to the characteristics of a person having ordinary skill in the art ("PHOSITA"). In particular, while Abbott identifies the PHOSITA as an individual with a medical or pharmacological background, Lupin adds that the person may instead be a formulator. Neither party argues that the Court must resolve this dispute in order to determine the appropriate construction of the disputed claim terms. This is so even with respect to the "treatment-limiting terms." Even if the PHOSITA is a formulator – who presumably would have no experience with treating patients for hyperlipidemia and, therefore, could not herself practice a patent having the claim limitations proposed by Abbott (which may require medical decisions made by physicians treating specific patients) – a formulator would be free to consult with others who are skilled in the art (if necessary) to understand treatment-limiting effects. (Tr. at 135) Also, as Lupin acknowledges, a PHOSITA need not be able to measure the elevations in liver enzymes herself. (Tr. at 119)

liver damage, uric acid increases, or elevations in fasting glucose levels," "little or no serious liver damage," and "no treatment-limiting hepatotoxicity" in substantially the same manner is undermined by other positions Lupin advocates. This is because Lupin agrees that the first two of these terms – despite using different language and appearing in different, yet related, patents – *should* have the same meaning. (D.I. 54 at 27) Lupin relies on *Kara Tech.*, 582 F.3d at 1347, for the proposition that "[w]here there are *significant differences* in claim language in the same family of patents, the Federal Circuit has given effect to those differences." (D.I. 54 at 26 (emphasis added)) Lupin has not, however, explained why the difference between the first two terms listed above and the third are great enough to warrant different interpretations, while the difference between the first and second terms are not enough. Further, when arguing that the '930 patent should be interpreted to exclude an internal hydrophobic component, Lupin correctly acknowledged that claim differentiation is not a "hard-and-fast" claim construction rule. (D.I. 60 at 11) Here, the different terms are being used in related patents but to mean the same thing.

Turning to the "treatment-limiting" terms in the '930 and '967 patents, for the same reasons already given in connection with claim 3 of the '428 patent and claim 3 of the '848 patent, I recommend that the Court not import the specific numerical limitations proposed by Lupin. Additionally, even though the '930 inventor stated that the "treatment-limiting" phrases in the '930 patent claims "mean or refer to that level or range which is not or would not be acceptable to the [FDA]," I do not view this as a clear, unambiguous, unmistakable disclaimer of all amounts that trigger even a single abnormal result for a single patient above the FDA range. *See generally Elbex Video*, 508 F.3d at 1372. The specification discloses that some patients in the Niaspan® clinical trials experienced glucose levels above the disclosed tables' upper limits

but were not withdrawn from the study. ('930 patent, col. 13 lines 25-60) Also, the Examiner himself was uncertain about the meaning of "treatment-limiting abnormalities," even after reviewing the applicant's statement quoted above. (D.I. 62, JA000961, '930 File History, Nov. 23, 1998 Office Action Summary at 3) Yet the claims were ultimately allowed with the "treatment-limiting" language intact and without further explanation. (D.I. 55 at 20)

Moreover, although Lupin argues that "treatment-limiting" does not give the public sufficient notice of the bounds of the claims' scope, here, reliance on the informed medical judgment of a trained physician in the relevant art is notice enough. *See, e.g.*, *Astra Aktiebolag v. Andrx Pharms., Inc.*, 222 F. Supp. 2d 423, 481 (S.D.N.Y. 2002) (construing "therapeutically effective amount" to mean "an amount that is effective for therapy" and explaining that "[a]n amount that is effective in therapy . . . will depend, among other things, on the individual"), *aff'd sub nom. In re Omeprazole Patent Litig.*, 2003 U.S. App. LEXIS 24899 (Fed. Cir. Dec. 11, 2003).

However, I do not agree with Abbott that the phrases "clinically significant" and "repeatedly" should be included in the constructions of the disputed terms in the claims of the '930 and '967 patents. While it seems likely that a physician would typically require "clinically significant" and "repeated" elevations before discontinuing or limiting a patient's treatment, in the context of these patents the important issue is whether the side effects are such that the physician and patient decide to limit or discontinue the patient's treatment. If this decision, for a particular patient, is reached without the presence of "clinically significant" or "repeated" elevations, the amount of hepatotoxicity that caused this decision is, within the meaning of these patents, "treatment-limiting."

Therefore, I recommend the following construction of the disputed claim terms in the '930 and '967 patents:

Disputed Term/Phrase	Recommended Construction
"abnormalities in either uric acid or glucose levels or both to an extent which would require said daily treatment to be discontinued by the patient" ('930 patent, claim 51) **"treatment-limiting . . . elevations in uric acid levels or glucose levels or both in the patient to a level which would require said treatment to be discontinued by the patient"** ('930 patent, claim 115)	Elevations in either uric acid levels, glucose levels or both to a level that requires discontinuation of current treatment
"treatment-limiting (i) hepatotoxicity . . . which would require said treatment to be discontinued by the patient" ('930 patent, claim 115)	Elevations in liver enzymes (AST, ALT, and/or alkaline phosphatase) to a level that requires discontinuation of current treatment
"treatment-limiting hepatotoxicity . . . in the individual to a level which would require use of the intermediate nicotinic acid formulation by the individual to be discontinued" ('967 patent, claim 16)	Elevations in liver enzymes (AST, ALT, and/or alkaline phosphatase) to a level that requires discontinuation of current treatment
"treatment-limiting elevations in uric acid or glucose levels or both in the individual to an level which would require use of the intermediate nicotinic acid formulation by the individual to be discontinued" ('967 patent, claim 16)	Elevations in either uric acid levels, glucose levels or both to a level that requires discontinuation of current treatment

C. "Sustained release composition" and "Oral sustained release solid dosage form"

Term/Phrase (Claim Nos.)	Abbott's Proposed Construction	Lupin's Proposed Construction
"sustained release composition" ('930 patent, claims 18 & 133)	A composition which when administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release formulations	A composition not containing an internal hydrophobic component designed to release an active ingredient slower than an immediate release formulation
"oral sustained release solid dosage form" ('930 patent, claims 51 & 115)	A drug product sold in a solid form to be administered by mouth and which when so administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release formulations	A solid dosage form not containing an internal hydrophobic component designed for oral administration and designed to release an active ingredient slower than an immediate release formulation

i. The Parties' Positions

In addition to the question of whether to import the limitation "no internal hydrophobic component," which has already been addressed, claims 18, 51, 115, and 133 of the '930 patent present another question: how to construe the "sustained release" elements of the terms. Abbott's suggested construction is taken from the '930 patent's specification, which defines "sustained release" as "a composition which when orally administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time." ('930 patent, col. 3 lines 63-67) The '930 specification also states that, compared to immediate release products, "[s]ustained release formulations are designed to slowly release the compound." ('930 patent, col. 1 lines 58-60) Lupin's proposed construction – "designed to release an active

ingredient slower than an immediate release formulation" – does not appear to be materially different than Abbott's proposal. Lupin did not, in either its briefing or during the *Markman* hearing, address this distinction between its proposal and Abbott's.

ii. Recommended Construction

I recommend that the Court adopt Abbott's proposed construction of claims 18, 51, 115, and 133 of the '930 patent. Abbott's proposed construction of "sustained release" comports with the specification's definition of "sustained release" as well as its plain and ordinary meaning.

D. "Significant increase in HDL cholesterol"

Term/Phrase (Claim Nos.)	Abbott's Proposed Construction	Lupin's Proposed Construction
"significant increase in HDL cholesterol" ('848 patent, claim 1)	No construction needed. If construed, then: "substantial increase in the level of HDL cholesterol in the patient's blood."	A 20% increase or greater in a patient's HDL profile.

i. The Parties' Positions

The dispute over the meaning of "significant increase" in claim 1 of the '848 patent again revolves around whether the Court should import a specific numerical limitation found in the portion of the '848 patent's specification describing the results of Niaspan® clinical trials.

Abbott argues that no construction is needed for this phrase because courts have repeatedly recognized that "terms of degree such as 'significant' or 'substantial' are descriptive terms not susceptible to precise numerical limitations." (D.I. 55 at 38 (citing *Playtex Prods., Inc. v. Procter & Gamble Co.*, 400 F.3d 901, 907 (Fed. Cir. 2005); *Anchor Wall Sys. v. Rockwood Retaining Walls, Inc.*, 340 F.3d 1298, 1310-11 (Fed. Cir. 2003); *Johnson & Johnson Vision Care,*

Inc. v. CIBA Vision Corp., 540 F. Supp. 2d 1233, 1269 (M.D. Fla. 2008))) Abbott also argues that the specification offers no support for Lupin's proposed numerical limits, which appear to be based on a mean increase in HDL levels of 23% and 25.3%, respectively. (*Id.* at 39) According to Abbott, there is no evidence that the inventor intended to claim a particular percentage that the HDL levels must exceed to be "significant;" indeed, David Bova rejected any rigid numerical threshold. (*Id.*; *see also* D.I. 58 at 35; D.I. 61, LA000467-68, Bova Dep. at 147-48) Additionally, Abbott notes that original claim 1 of the '848 patent contained this term ("significant increase") and it issued without amendment. (D.I. 58 at 35) Finally, Abbott asserts that its expert, Dr. Sacks, confirms that a person of ordinary skill in the art would understand that "whether a particular increase in HDL cholesterol is 'significant' is patient specific," and that "[i]n some patients an increase of considerably less than 20% would be deemed 'significant' if it contributes to a lowering of the individual's risk of developing cardiovascular disease." (*Id.* (citing Sacks Decl. ¶ 40))

Lupin, on the other hand, observes that the specification states that dosing with a sustained release product once a day in the evening or at night achieves a "significant" reduction in LDL cholesterol and triglycerides along with a "significant increase" in the desired HDL cholesterol. (D.I. 54 at 22 (citing '848 patent, col. 3 lines 35-40)) To Lupin, the meaning of "significant" is set forth in the Niaspan® clinical trial results listed in Table II; specifically, the specification notes that 13 out of 25 patients who had increases of HDL cholesterol of over 20% had "significant" "increases" in HDL cholesterol. (*Id.* (citing '848 patent, col. 9 lines 59-60)) Lupin's proposed 20% threshold for "significant" is lower than the increases actually referred to in the supporting study, and is roughly the average from the study discussed in the patent's

Background section. (*Id.* (citing '848 patent, col. 2 lines 5-18)) Lupin insists that its construction avoids the vagueness inherent in Abbott's proposal, fulfilling the specification's express goal of providing SR products with "balanced lipid alteration" between prior art IR and SR products. (*Id.* at 23)

ii. Recommended Construction

I recommend that the Court construe "significant increase in HDL cholesterol" as "an increase in HDL cholesterol that results in a meaningful decrease in an individual's risk of developing cardiovascular disease."

As an initial matter, the word "significant," as used in the disputed claim term, does require construction. The '848 patent's specification implicitly links "significant" to average increases in HDL cholesterol of 23% and 25.3%, but it gives no guidance regarding which number should determine the meaning of "significant." ('848 patent, col. 9 lines 53-60) I agree with Abbott that the inventor wanted to avoid limiting this claim to a specific numerical threshold. (*See generally* D.I. 61, LA000467-68, Bova Dep. at 147-48.) The inventor, Bova, testified that the disputed phrase would mean a "clinically significant or statistically significant increase" compared to the baseline/placebo, and that "[c]linically significant would mean have a positive effect on cardiovascular risk." (*Id.*) The inventor's testimony is consistent with Dr. Sacks' discussion of how a person ordinarily skilled in the art would understand the term.[25] (Sacks Decl. ¶¶ 39-40) Additionally, I am persuaded that, as Dr. Sacks notes, the meaning of "significant increase in HDL cholesterol" will vary from patient to patient, in large part because

[25]With respect to Lupin's criticism of Dr. Sacks' declaration for not citing the patents' specifications, I note that none of the four expert affidavits submitted by Lupin do so either. *See* D.I. 61, LA000670-78, LA000679-84, LA000964-67, LA000968-72.

patients have individual baseline levels of HDL cholesterol and individual medical histories and conditions that must be taken into account. Also, I am unpersuaded by the specific numerical requirement that Lupin would impose – for the same reasons already described in reference to the treatment-limiting claim terms.

As Dr. Sacks and Bova point out, an increase in HDL cholesterol is considered significant because it reduces a patient's risk for cardiovascular disease. (*See id.*; D.I. 61, LA000467-68, Bova Dep. at 147-48) Thus, I conclude that a person ordinarily skilled in the art would understand the disputed term to mean "an increase in HDL cholesterol that results in a meaningful decrease in an individual's risk of developing cardiovascular disease."

E. "Intermediate release nicotinic acid formulation"

Term/Phrase (Claim Nos.)	**Abbott's Proposed Construction**	**Lupin's Proposed Construction**
"intermediate release nicotinic acid formulation" ('229 patent, claims 17 & 25) ('691 patent, claim 13) ('715 patent, claims 1, 3, 5, 7, 9, & 11) ('967 patent, claim 16)	A nicotinic acid formulation which, when administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release niacin formulations, but faster and different than other sustained release niacin formulations	A dosage form not containing an internal hydrophobic component that releases an active ingredient, namely, nicotinic acid, in vitro or in vivo over a period of time which is greater than 1 hour but less than 24 hours

i. The Parties' Positions

With respect to the proper understanding of the temporal aspect of the disputed phrase, Abbott observes that the CIP patents' specifications all state that:

> As indicated herein, "intermediate release" is understood to mean a composition or formulation which, when orally administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of IR niacin formulations, but faster and different than SR niacin products.

('229 patent, col. 16 lines 33-40; '691 patent, col. 16 lines 30-38; '715 patent, col. 17 lines 2-9; '967 patent, col. 17 lines 2-9) The same specifications also state:

> "[I]ntermediate release" . . . is used herein to characterize the nicotinic acid formulations of the present invention which release their medication in vitro or in vivo over a period of time which is greater than about 1 to 2 hours, *i.e.*, slower than IR niacin, but less than about 10 to 24 hours, *i.e.*, faster than SR niacin.

('229 patent, col. 5 lines 33-39; '691 patent, col. 5 lines 35-41; '715 patent, col. 5 lines 35-41; '967 patent, col. 5 lines 31-37) Abbott denies that the latter description's numerical high and low endpoints should control (as they do in Lupin's construction), however, because the very purpose of using numerical time periods and the word "about" in describing them – as opposed to fixed endpoints – is to avoid numerical certainty. Abbott attests that "[i]t is axiomatic that the term 'about' avoids strict numerical limitations." (D.I. 55 at 43-44 n.9 (citing *Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1368 (Fed. Cir. 2008))

Lupin responds that the second quotation shown above should control, since it is more specific than the first. (D.I. 60 at 17) Additionally, the word "about" is not in the actual claim language being construed, just in the specifications, so precedents construing "about" as a claim term are inapposite. (*Id.* at 16) Lupin also objects that Abbott's proposed construction is ambiguous because it lacks limits. (*Id.* at 17) For example, the phrase "faster and different than other sustained release niacin formulations" in Abbott's proposal is ambiguous because there is

no specified standard for assessing "different," and "other sustained release formulations" could refer to any number of SR products, including those disclosed in the specification, those marketed at the time of the patent's issuance, or even those marketed at any time in the future. (*Id.* at 18) By contrast, Lupin insists that its proposed construction provides certainty and reflects the full range of time periods suggested in the CIP patents' specifications.

ii. Recommended Construction

I have concluded that neither Abbott nor Lupin has properly construed the disputed claim term "intermediate release nicotinic acid formulation." Instead, I recommend that the Court construe this term as "a nicotinic acid formulation which, when administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is greater than about 1 to 2 hours, *i.e.*, slower than immediate release niacin, but less than about 10 to 24 hours, *i.e.*, faster than sustained release niacin."[26]

This recommended construction is derived from the two specification excerpts quoted above, in which the inventor essentially defines the term "intermediate release" for purposes of the claims of these patents. The specifications' definitions are consistent with one another. Combining them, as I recommend, eliminates the ambiguity identified by Lupin in the phrase "different than other sustained release formulations." Additionally, while "about" does not appear in the disputed claim, it is appropriate here to include it in the construction, as it is part of the specifications' definitions. "About" is used in the specifications to show that the time periods within which SR and IR products are released vary based on metabolic factors and are

[26]For the reasons discussed previously, I do not believe the CIP patent claims (like those of the other claims in dispute) should be construed to include the limitation "not containing an internal hydrophobic component.

thus difficult to predict, as is well known by those skilled in the art. (*See, e.g.*,. '715 patent, col. 1 lines 54-67 ("[IR] nicotinic acid formulations generally release nearly all of their nicotinic acid within about 30 to 60 minutes following ingestion . . . . [SR] nicotinic acid formulations are designed to release significant quantities of drug for absorption into the bloodstream . . . over an extended period such as 12 or 24 hours after ingestion."); *id.* col. 4 lines 34-37 ("The difficulty of correctly predicting the appropriate release pattern [for SR products] is well known to those of skill in the art.").)

F. "About"[27]

Term/Phrase (Claim Nos.)	**Abbott's Proposed Construction**	**Lupin's Proposed Construction**
Category I: "Dose Amount" limitations		
"about 1000 mg" ('715 patent, claims 1, 3, 5, 7, & 9) ('967 patent, claim 16 (1000 mg only))	Approximately 1000 mg	No less than 850 mg and no more than 1150 mg
"at least about 750 mg" ('229 patent, claims 17 & 25)	No less than approximately 750 mg	No less than 637.5 mg
Category II: "Blood Plasma Concentration and Urinary-Metabolite-Profile" limitations		
"about 4.0% to about 26%" ('715 patent, claims 1, 5, & 9)	Approximately 4.0% to approximately 26%	No less than 3.6% to no more than 28.6%
"about 3 ug/ml" ('229 patent, claims 17 & 25)	Approximately 3 ug/ml	No less than 2.7 ug/ml
"about 5.6 hours" ('229 patent, claims 17 & 25)	Approximately 5.6 hours	No less than 5.04 hours

[27]An example for each type of "about" term is provided. See D.I. 55 at 46 for the comprehensive list.

"about 11 ughr/ml" ('229 patent, claims 17 & 25)	Approximately 11 ughr/ml	No less than 9.9 ughr/ml
Category III: "Dissolution Profile" limitations		
"about 15%" **"about 15 % and about 30%"** **"about 75%"** ('967 patent, claim 16) ('691 patent, claim 13)	Approximately 15% Approximately 15% and approximately 30% Approximately 75%	At least 13.5% Between 13.5 % and 33% Not above 82.5%
Category IV: "Fit Factor F2" limitations		
"about 44" ('967 patent, claim 16) ('691 patent, claim 13)	Approximately 44	No less than 43.5

i. The Parties' Positions

The central dispute regarding the "about" claim terms in the CIP patents is whether a person ordinarily skilled in the art would read those terms in reference to the United States Pharmacopeia ("USP"), a "non-governmental, official public standards-setting authority, which sets and publishes quality . . . and consistency standards, as well as verification standards for . . . prescription and over-the-counter medicines, other health care products, food ingredients, and dietary supplements." (D.I. 58 at 36-37 & n.18) (internal citation omitted)

Abbott contends that nowhere in the claims or specification is there an indication that the inventor intended to depart from the general principle that "about" avoids a strict numerical limitation. (D.I. 55 at 47-48 (citing *Cohesive Techs.*, 543 F.3d at 1368; *Verve, LLC v. Crane*

Cams, Inc., 311 F.3d 1116, 1120 (Fed. Cir. 2002))) Abbott argues that where, as here, the patentee did not clearly redefine the word, "about" should be given its ordinary and customary meaning of "approximately." (*Id.* at 47-48 (citing *Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364, 1369-72 (Fed. Cir. 2005); *UCB, Inc. v. KV Pharm. Co.*, 2009 U.S. Dist. LEXIS 72764, at *15 (D. Del. Aug. 18, 2009); *Unigene Labs., Inc. v. Apotex Inc.*, 2008 U.S. Dist. LEXIS 66005, at *26-27 (S.D.N.Y. Aug. 28, 2008))) Additionally, according to Abbott, a person ordinarily skilled in the art would understand that "about" means "approximately," because the term "about" "reflects the inherent uncertainty in any scientific measurement – *i.e.*, repeated measurements of the same property will not yield exactly the same result due to the limitations of accuracy and precision associated with measurement and testing techniques." (*Id.* at 49 (citing D.I. 56, AA Ex. A, ("Foster Decl.") ¶ 56 and McGinity Decl. ¶¶ 63-66))

With respect to whether an ordinarily skilled artisan would refer to the USP to define the "about" terms in the CIP patent claims, Abbott argues that she would do so only for the particular purpose specified in the CIP patents. (D.I. 58 at 37-39 & n.19) The CIP patents' specifications all include a single reference to the USP:

> Each nicotinic acid formulation of the instant invention will typically exhibit the following dissolution profile in U.S.P. XXIII, Apparatus I, 900 mls of deionized water at 37°C., baskets at 100 RPM, as indicated in Table 3.

(*E.g.*, '229 patent, col. 9 lines 13-16) The claims of the '691 and '967 patents also reference the USP in connection with this same "type I dissolution apparatus." ('691 patent, claims 1, 13 (referring to "a type I dissolution apparatus (basket) according to [USP XXII]"); '967 patent, claims 1, 16 (same)) According to Abbott, there is no reference to the USP in connection with

any other aspect of the CIP claims. (D.I. 58 at 38) Thus, an ordinarily skilled artisan would know that the USP should be consulted to determine the parameters of the "about" claims in the '691 and '967 patents because those particularly refer to measuring an *in vitro* (i.e., laboratory testing) dissolution profile. (*Id.* at 38 n.19)

Relying on the USP for other uses, Abbott continues, would be inappropriate because most of the contexts in which "about" appears are related to parameters that the USP does not govern. (*Id.* (citing D.I. 56 AA Ex. E, Supplemental Foster Decl. ("Supp. Foster Decl.") ¶¶ 16-28)) The USP sets performance standards for *in vitro* parameters of drug quality, purity, and consistency between batches. (Supp. Foster Decl. ¶¶ 8, 10) The USP does not, as Lupin suggests, set standards for *in vivo* (i.e., biological) parameters, such as pharmacokinetics or bioequivalence. (*Id.* ¶ 10) Thus, a person ordinarily skilled in the art would not have looked to the USP in the context of *in vivo* measurements, such as the plasma concentration parameters of the '229 patent or the urinary metabolic profile parameters of the '715 patent. (*Id.* ¶¶ 24-28) In Abbott's view, a person ordinarily skilled in the art would not even have looked to the USP for guidance regarding *in vitro* parameters, other than the specific parameter for the "type I dissolution apparatus" disclosed in the '691 and '967 patents, because she would have understood "about" to mean "approximately." (*Id.* at 39-40 (citing Supp. Foster Decl. ¶¶ 14-23))

Lupin, by contrast, argues that the "technological and stylistic context" of the "about" terms dictates that the USP parameters be consulted. (D.I. 54 at 28-29 (citing *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217 (Fed. Cir. 1995))) The CIP patents concern the fields of pharmaceutics (creating an appropriate dosage form for a drug) and biopharmaceutics. (*Id.* (citing '229 patent, col. 7 line 50 to col. 16 lines 1-27)) Lupin acknowledges that absolute

precision in measuring active ingredient weights and concentrations in blood plasma and urine is not possible in these fields. (*Id.* at 29) However, boundaries of weights and *in vivo* concentrations can still be set, and are necessary to distinguish the CIP dosage forms from prior-art SR dosage forms. (*Id.* (citing D.I. 56, LA000683-84, Taft Declaration (hereinafter "Taft Decl.") ¶¶ 10-11))

Lupin's expert, Dr. Taft, declares that in the fields of pharmaceutics and biopharmaceutics, using "about" to modify a numerical range is understood to refer to a deviation acceptable around a particular data point. (Taft Decl. ¶¶ 10-12; *see also* D.I. 60 at 34-38 (discussing general agreement among Dr. Cefali, an inventor of most of the CIP patents, David Bova, Lupin's expert, Dr. Taft, and Abbott's experts, Drs. McGinity and Foster, that there is "inherent variability" in the manufacturing process based on the particular equipment used and/or accuracy of assay method).) Lupin argues that the numerical ranges in almost all of its proposed constructions represent the accepted variance percentages found in the USP XXII and USP XXIII, which were in effect at the time of the invention. (D.I. 60 at 32-38)

According to Lupin, the only numerical ranges that are not derived from a version of the USP are with respect to claim 13 of the '691 patent and claim 16 of the '967 patent, both of which require a particular "fit factor F_2" for comparing a test dissolution profile to a reference dissolution profile. (D.I. 54 at 41-43) Lupin proposes that a "fit factor F_2" of "about 44" should be construed as "no less than 43.5" because numbers between 43.5 and 43.9 round to the nearest whole number, which is 44. (*Id.* at 42 (citing *San Huan New Materials High Tech., Inc. v. Int'l Trade Comm'n*, 161 F.3d 1347, 1361 (Fed. Cir. 1998)) According to Lupin, nothing in the '691 or '967 patents' specifications or prosecution histories warrants departing from this "standard

scientific convention." (*Id.* (citing *Viskase Corp. v. Am. Nat'l Can Co.*, 261 F.3d 1316, 1320-21 (Fed. Cir. 2001))

ii. Recommended Construction

I recommend different constructions for each set of "about" claims in dispute, as follows.

a. Claims regarding "dose-amount limitations" in the '229, '715, and '967 patents

I recommend that the Court adopt Lupin's proposed construction of "about" for the dose-amount limitations claims in the '229, '715, and '967 patents. The "dose-amount" limitations claims are claims 17 and 25 of the '229 patent; claims 1, 3, 5, 7, and 9 of the '715 patent; and claim 16 of the '967 patent. (D.I. 54 at 29-30) Both parties agree that a person ordinarily skilled in the art would look to the USP for guidance on these issues, and the patent's inventors and all the experts agree that "about" in these claims essentially means within the range of scientifically acceptable error. Given that the USP edition in effect at the time of the invention set the standards for such scientifically acceptable manufacturing errors in pharmaceutical preparations, a person ordinarily skilled in the art would have consulted the USP to determine the meaning of "about." Abbott, however, objects that the USP XXIV – which is not the one in effect at the time of the invention – has a specific tablet strength tolerance for niacin compositions, which is +/- 10%, rather than the "general" tolerance of +/- 15%. (D.I. 58 at 39 n.21) There is nothing in the record as to whether the USP XXII and XXIII – the versions of the USP that were in effect at the time the patents were being prosecuted – also had a specific tolerance for niacin compositions. In the absence of such evidence, I recommend that the Court construe the "dose-amount limitations" in accordance with Lupin's proposed construction (i.e., +/- 15%).

b. Claims regarding Blood Plasma Concentration limitations and Urinary-Metabolite-Profile limitations in the '229 and '715 patents

With respect to the blood plasma concentration limitations and Urinary-Metabolite-Profile limitations in the '229 and '715 patents, I recommend that the Court adopt Abbott's construction of "about" in claims 17 and 25 of the '229 patent and claims 1, 5, and 9 of the '715 patent. Abbott's assertion that the USP standards are not designed to apply to *in vivo* parameters, such as blood plasma concentrations and urinary metabolite profiles, appears to be supported by Lupin's expert, Dr. Taft. (D.I. 61, LA000971-981, Supplemental Taft Declaration ("Supp. Taft Decl.") ¶¶ 6- 8) Although agreeing with Abbott's expert that repeated measurements of blood plasma concentrations may not yield the same results, Dr. Taft states that "the results should be reproducible to within an acceptable degree of error. In my opinion, an acceptable degree of error is +/- 10%." (Supp. Taft Decl. ¶ 6) He goes on to state that the USP provides guidance for "performance characteristics" of the analytical methods used to measure "drug and, in some cases, metabolite(s) in plasma and/or urine." (*Id.* ¶ 7) However, "the USP does not specify an acceptable limit of variability in these performance characteristics," which themselves are but one aspect of verifying that a test for blood plasma concentration or urinary metabolites is accurate. (*Id.* ¶¶ 6, 8) Dr. Taft notes that "+/- 10% is supported by *the scientific literature*, specifically for published methods used to measure niacin," and cites the results of two studies that described their variation in reproducability results as at or below 10%. (*Id.* ¶ 8 (emphasis added))

Thus, it seems that not even Lupin's own expert believes that the USP provides the proper guidelines for measuring blood plasma concentrations and urinary metabolite profiles. In

fact, Dr. Taft's reliance on "scientific literature" and other studies indicates that what he is really basing his opinion on is what a person ordinarily skilled in the art would rely upon – namely, the body of available published literature and conventions in the art. In these circumstances, Abbott's construction of "about" as "approximately" reflects the ordinary and customary meaning of the term as understood by a person ordinarily skilled in the art and is more appropriate than Lupin's more specific numerical range.

c. Dissolution profile claims in the '691 and '967 patents

Both parties recognize that claim 13 of the '691 patent and claim 16 of the '967 patent expressly reference USP standards for measuring an *in vitro* dissolution profile. (D.I. 58 at 38 n.19; D.I. 54 at 40) Although "about" generally avoids a "strict numerical boundary to the specified parameter," it must still be interpreted according to the patent's field and specification, and can be narrowed where the specification allows it. *Cohesive Techs.*, 543 F.3d at 1368-69.

In *Cohesive Techs.*, 543 F.3d at 1368-69, the Federal Circuit construed "about 30 [mu] m" as "between 25.434 [mu] m and 34.566 [mu] m" because the specification provided the precise means of doing so. Specifically, another part of the specification treated "about 50 [mu] m" as if it were the same as "42.39 [mu] m." *Id.* This deviation from the exact number 50 represented an "acceptable variance of at least 15.22%." *Id.* Therefore, the court applied a 15.22% variance to the "about 30 [mu] m" term and decided it should encompass "at least 25.434 [mu] m but not more than 34.566 [mu] m." *Id.*

Similarly, here, before reciting a litany of percentage ranges using the term "about," the '691 and '967 patents teach that the *in vitro* dissolution profile to be used in the invention should be measured according to USP XXII's standards. ('691 patent, col. 30 lines 13-33; '967 patent,

col. 30 lines 43-62) The claims of the '691 and '967 patents also reference the USP in connection with this same "type I dissolution apparatus." ('691 patent, claims 1, 13; '967 patent, claims 1, 16) Therefore, I recommend that the Court adopt Lupin's proposed construction of "about" in claim 13 of the '691 patent and claim 16 of the '967 patent, because it comports with express claim language and would be understood by a person ordinarily skilled in the art to require consultation of the USP XXII standards for dissolution profiles.

d. "Fit factor F_2" claims in the '691 and '967 patents

With respect to the meaning of "about" in the "fit factor F_2" claims – claim 13 of the '691 patent and claim 16 of the '967 patent – I recommend that the Court adopt Lupin's proposed constructions. In *Viskase Corp.*, 261 F.3d at 1321, the Federal Circuit reversed a district court that construed the term "about 0.91 g/cm3" to mean densities between 0.905 and 0.914 based on the reasoning that numbers in that range would be rounded to 0.91. Although the Federal Circuit agreed that this practice "is a standard scientific convention when a number has not been carried to the next mathematically significant figure," it construed the term "below about 0.91 g/cm3" as "below about 0.910 g/cm3." *Id.* at 1322. It did so in large part because the inventor had used the density figure "0.910" during prosecution to distinguish prior art, even though the claims themselves only recited "0.91." *Id.* at 1321-22. In this way the inventor had signaled that it was important to describe the numbers out to three decimal places.

Here, the '691 and '967 patents' specifications explain that the range of potential "fit factor F_2[s]" will be a "number between 0 and 100." ('691 patent, col. 11 lines 17-62; '967 patent, col. 11 lines 35-63) However, the patents list recommended fit factor F_2 values (for both Niaspan® and competitor products) using numbers described to the first decimal place, *e.g.* "+/-

79.0" for Niaspan®, and "54.3" for a competitor's product. This indicates that the inventors intended that the fit factor F_2 values be described to the first decimal place. Lupin's construction accommodates that intention.

RECOMMENDED CONSTRUCTIONS

For the reasons set forth above, I recommend that the Court construe the disputed claim terms as follows:

Term/Phrase (Claim Nos.)	Recommended Construction
"Oral solid dosage form" ('428 patent, claim 1)	A drug product in a solid form to be administered by mouth
"sustained release composition" ('930 patent, claims 18 & 133)	A composition which when administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release formulations
"oral sustained release solid dosage form" ('930 patent, claims 51 & 115)	A drug product sold in a solid form to be administered by mouth and which when so administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release formulations
"dosing" ('848 patent, claim 1)	Administering a dose
"intermediate release nicotinic acid formulation" ('715 patent, claims 1, 3, 5, 7, 9, & 11) ('967 patent, claim 16) ('691 patent, claim 13) ('229 patent, claims 17 & 25)	A nicotinic acid formulation which releases its medication in vitro or in vivo over a period of time which is greater than about 1 to 2 hours, *i.e.*, slower than immediate release niacin, but less than about 10 to 24 hours, *i.e.*, faster than sustained release niacin

Term/Phrase (Claim Nos.)	Recommended Construction
"little or no serious liver damage" ('428 patent, claim 3)	No treatment-limiting hepatotoxicity that would require treatment to be discontinued by the patient
"minimum liver damage, uric acid increases, or elevations in fasting glucose levels" ('848 patent, claim 3)	No treatment-limiting hepatotoxicity or elevations in uric acid levels or glucose levels which would require treatment to be discontinued by the patient
"abnormalities in either uric acid or glucose levels or both to an extent which would require said daily treatment to be discontinued by the patient" ('930 patent, claim 51) **"treatment-limiting . . . elevations in uric acid levels or glucose levels or both in the patient to a level which would require said treatment to be discontinued by the patient"** ('930 patent, claim 115)	Elevations in either uric acid levels, glucose levels or both to a level that requires discontinuation of current treatment
"treatment-limiting (i) hepatotoxicity . . . which would require said treatment to be discontinued by the patient" ('930 patent, claim 115)	Elevations in liver enzymes (AST, ALT, and/or alkaline phosphatase) to a level that requires discontinuation of current treatment
"treatment-limiting hepatotoxicity . . . in the individual to a level which would require use of the intermediate nicotinic acid formulation by the individual to be discontinued" ('967 patent, claim 16)	Elevations in liver enzymes (AST, ALT, and/or alkaline phosphatase) to a level that requires discontinuation of current treatment
"treatment-limiting elevations in uric acid or glucose levels or both in the individual to an level which would require use of the intermediate nicotinic acid formulation by the individual to be discontinued" ('967 patent, claim 16)	Elevations in either uric acid levels, glucose levels or both to a level that requires discontinuation of current treatment

Term/Phrase (Claim Nos.)	Recommended Construction
"sustained release composition" ('930 patent, claims 18 & 133)	A composition which when administered to a patient to be treated, the active ingredient will be released for absorption into the blood stream over a period of time which is slower than that of immediate release formulations
"significant increase in HDL cholesterol" ('848 patent, claim 1)	An increase that results in a meaningful decrease in an individual's risk of developing cardiovascular disease
"about 1000 mg" ('715 patent, claims 1, 3, 5, 7, & 9) ('967 patent, claim 16 (1000 mg only))	No less than 850 mg and no more than 1150 mg
"about 4.0% to about 26%" ('715 patent, claims 1, 5, & 9)	Approximately 4.0% to approximately 26%
"at least about 750 mg" ('229 patent, claims 17 & 25)	No less than 637.5 mg
"about 3 ug/ml" ('229 patent, claims 17 & 25)	Approximately 3 ug/ml
"about 5.6 hours" ('229 patent, claims 17 & 25)	Approximately 5.6 hours
"about 11 ughr/ml" ('229 patent, claims 17 & 25)	Approximately 11 ughr/ml

Term/Phrase (Claim Nos.)	Recommended Construction
"about 15%" **"about 15% and about 30%"** **"about 75%"** ('967 patent, claim 16) ('691 patent, claim 13)	At least 13.5% Between 13.5% and 33% Not above 82.5%
"about 44" ('967 patent, claim 16) ('691 patent, claim 13)	No less than 43.5

This Report and Recommendation is filed pursuant to 28 U.S.C. § 63(b)(1)(B), Fed. R. Civ. P. 72(b)(1), and D. Del. LR 72.1. The parties may serve and file specific written objections **of no longer than ten (10) pages within fourteen (14) days after being served with a copy of this Report and Recommendation. Fed. R. Civ. P. 72(b).** The failure of a party to object to legal conclusions may result in the loss of the right to de novo review in the district court. *See Henderson v. Carlson*, 812 F.2d 874, 878-79 (3d Cir. 1978); *Sincavage v. Barnhart*, 171 Fed. Appx. 924, 925 n.1 (3d Cir. 2006). **A party responding to objections may do so within fourteen (14) days after being served with a copy of objections; such response shall not exceed ten (10) pages. No further briefing shall be permitted with respect to objections without leave of the Court.**

The parties are directed to the Court's Standing Order In Non-Pro Se Matters For Objections Filed Under Fed. R. Civ. P. 72(b), dated November 16, 2009, a copy of which is available on the Court's website, www.ded.uscourts.gov/StandingOrdersMain.htm.

Dated: June 18, 2010
Wilmington, Delaware

Honorable Leonard P. Stark
UNITED STATES MAGISTRATE JUDGE