IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

SHIRE LLC et al, Plaintiffs,	:	
v.	:	Civil Action No. 10-329-RGA
TEVA PHARMACEUTICALS USA INC. et al, Defendants.	:	

Francis DiGiovanni, Esq., Wilmington, Delaware, Edgar H. Haug, Esq. (argued), New York, New York, Attorneys for Plaintiffs.

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Dominick T. Gattuso, Esq., Wilmington, Delaware, Chad Landmon, Esq. (argued), Washington, D.C., Attorneys for Defendants Actavis Elizabeth LLC and Actavis Inc.

John C. Phillips, Jr., Esq., Wilmington, Delaware, Attorney for Defendants Anchen Pharmaceuticals, Inc. and Anchen Inc.

MEMORANDUM OPINION

March 21, 2012

ANDREWS, U.S. DISTRICT JUDGE:

Plaintiffs Shire LLC, Supernus Pharmaceuticals, Inc, Amy F.T. Arnsten, Pasko Rakic, and Robert D. Hunt filed this action against Defendants Teva Pharmaceuticals USA, Inc., Teva Pharmaceutical Industries, Ltd., Actavis Elizabeth LLC, Actavis Inc., Anchen Pharmaceuticals Inc., and Anchen Inc. alleging infringement of United States Patent Numbers 5,854,290 ("the '290 patent"), 6,287,599 ("the '599 patent"), and 6,811,794 ("the '794 patent"). The three patents are listed in the Food and Drug Administration's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaulations" as covering Intuniv®, a drug used to treat pediatric ADHD. A subset of Defendants filed Abbreviated New Drug Applications with the U.S. Food and Drug Administration, seeking approval of generic forms of Intuniv®. The parties briefed their respective positions on claim construction, and the Court conducted a *Markman* hearing. This Memorandum Opinion provides construction of the disputed terms.

The '290 patent, entitled "Use of guanfacine in the treatment of behavioral disorders," generally relates to the use of guanfacine to treat ADHD and Tourette's syndrome, without sedative side effects. The '599 patent, entitled "Sustained release pharmaceutical dosage forms with minimized pH dependent dissolution profiles," addresses pharmaceutical compositions having a pH-independent or a minimized pH-dependent dissolution profile. The '794 patent, also entitled "Sustained release pharmaceutical dosage forms with minimized pH dependent dissolution profiles," addresses the same pharmaceutical compositions as used to administer guanfacine hydrochloride and other drugs.

I. Claim Construction

Claim construction is a question of law. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 977–78 (Fed. Cir. 1995). When construing patent claims, a court considers the literal language of the claim, the patent specification and the prosecution history. *Id.* at 979. Of these

sources, the 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." *Phillips v. AWH Corporation*, 415 F.3d 1303, 1312–17 (Fed. Cir. 2005). However, "[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).

A court may consider extrinsic evidence, including expert and inventor testimony, dictionaries, and learned treatises, in order to assist it in understanding the underlying technology, the meaning of terms to one skilled in the art and how the invention works. *Phillips*, 415 F.3d at 1318–19; *Markman*, 52 F.3d at 979–80. But extrinsic evidence is considered less reliable and less useful in claim construction than the patent and its prosecution history. *Phillips*, 415 F.3d at 1318–19.

In addition to these fundamental claim construction principles, a court should also interpret the language in a claim by applying the ordinary and accustomed meaning of the words in the claim. *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 759 (Fed. Cir. 1984). If the patent inventor clearly supplies a different meaning, then the claim should be interpreted according to the meaning supplied by the inventor. *Markman*, 52 F.3d at 980. Finally, claims should be construed to avoid redundancy. *See Phillips*, 415 F.3d at 1324.

A. The '290 Patent: Use of Guanfacine in the Treatment of Behavioral Disorders

The '290 patent claims methods of treating disorders that have prominent symptoms of behavioral disinhibition (*e.g.*, ADHD and Tourette's Syndrome) with minimal sedative side effects by administering a therapeutically effective amount of guanfacine. '290 Patent, at [57]; *id.* col.12 ll.29-65.

1. *"without inducing excessive sedation"*

Independent claims 1 and 7 recite methods for addressing behavioral disinhibition "without inducing excessive sedation."

Plaintiffs' Proposed Construction	without inducing sedation to an extent that impairs functioning
Actavis' and Anchen's Proposed Construction	without inducing sedation to an extent equal to or greater than that which is associated with the administration of clonidine
Court's Construction	without inducing sedation to an extent that impairs functioning

The patent discloses that clonidine comprises prior art in the treatment of ADHD, but that it is associated with "significant adverse side effects, including . . . excessive sedation." '290 Patent, col.2 ll.5-16. Plaintiffs, Actavis, and Anchen agree that the '290 specification describes "excessive sedation" in the context of clonidine administration. (D.I. 95 at 14; D.I. 93 at 10-11). The patent repeatedly compares guanfacine's sedative effects to clonidine's. '290 Patent, col.3 ll.52-61; col.7 ll.33-36; col.4 ll.19-22; col.7, l.66- col.8, l.6; col., ll.48-59; col.9 ll.27-28; fig. 2B. The prosecution history also describes guanfacine as a less sedating alternative to clonidine. (D.I. 94-19, Sept. 2, 1997 Response to Office Action at 3). Sedation is described in terms of functional impairment. '290 Patent, col.2 ll.24-28; col.5 ll.15-22; col.6 ll.42-43; col.11 ll.42-65.

Defendants argue that these numerous comparisons indicate the claim term was intended to reflect the distinction between guanfacine's sedative side effects and clonidine's sedative side effects. (D.I. 93 at 20). Plaintiffs argue that the explanations and examples of sedative side effects from both guanfacine and clonidine, described in terms of functional impairment, indicate to one of ordinary skill that excessive sedation is to an extent that impairs functioning. (D.I. 95 at 12-15).

The patent discloses evaluating sedation in terms of functional impairment. '290 Patent, col.2 ll.24-28; col.5 ll.15-22; col.6 ll.42-43; col.11 ll.42-65. Sedation caused by clonidine is not always to an extent that impairs functioning; mere sedation is not equivalent to impaired functioning. *See id.* col.2 ll.40-44 ("[M]oderate do[s]es of clonidine . . . improve working memory performance in aged monkeys without hypotensive or sedative side effects."). The term "without inducing excessive sedation" is therefore construed to mean "without inducing sedation to an extent that impairs functioning."

2. *"readministering the dose at an interval required to obtain a desired level and duration of behavioral inhibition"*

Dependent claim 2 claims the method of claim 1 comprising the additional step of readministering a behavior inhibiting dose of guanfacine at an interval required to obtain a desired level and duration of behavioral inhibition.

Plaintiffs' Proposed Construction	administering an amount of guanfacine multiple times within a single day or on multiple days to obtain a desired degree and length of time of the improvement of self-control of behavior
Actavis' and Anchen's Proposed Construction	administering an amount of guanfacine multiple times within a single day or on multiple days to obtain any improvement of self-control of behavior over a longer period of time than would be achieved with a single administration of an amount of guanfacine
Court's Construction	administering an amount of guanfacine multiple times within a single day or on multiple days to obtain a therapeutic degree and length of time of the improvement of self-control of behavior

Plaintiffs propose modifying the degree and length of time of improvement with "desired," to permit a skilled artisan to set goals and evaluate outcomes with regard to behavioral disinhibition. (D.I. 103 at 6-7). Actavis and Anchen propose changing "desired level and duration" to "any improvement" and "longer period of time" to resolve ambiguity in the "desired" language. (D.I. 93 at 23). Actavis and Anchen also propose a comparison to a single guanfacine administration, drawing from a perceived comparison between Example 4's chronic

administration to human subjects and Examples 1, 2, and 3's single-dose administration to monkey subjects. *Id.* at 23-24.

Both proposals are problematic. Plaintiffs' construction does not provide any objective definition identifying a standard for determining when the degree and length of time of behavioral improvement has been reached. *See Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1350 (Fed. Cir. 2005). In the absence of a workable objective standard, "desired degree and length of time" is completely dependent on a person's subjective opinion. *See id.* "The scope of claim language cannot depend solely on the unrestrained, subjective opinion of a particular individual purportedly practicing the invention." *Id.*

Actavis' and Anchen's proposal of "any improvement . . . over a longer period of time than would be achieved with a single administration of an amount of guanfacine" is not supported by the patent. While Examples 1, 2, and 3 address single dose trials, and Example 4 discloses chronic administration, the patent does not disclose any comparison between the single dose and chronic dosage examples. There is no support for limiting the claim term by such a comparison. A limitation of "any improvement" reads the concept of a "desired" improvement out of the claim.

The Court construes this term as "administering an amount of guanfacine multiple times within a single day or on multiple days to obtain a therapeutic degree and length of time of the improvement of self-control of behavior." The specification describes readministration in terms of "therapeutic dosage" and "therapeutic administration." '290 Patent, col.5 ll.60-67. The patent uses the word "therapeutic" to more objectively convey the concept of a "desired improvement" in behavioral self-control.

B. The '599 and '794 Patents: Sustained Release Pharmaceutical Dosage Forms with Minimized pH Dependent Dissolution Profiles

The '599 and '794 patents address pharmaceutical compositions with minimized pH-dependent dissolution profiles or pH-independent dissolution profiles. '599 Patent, at [57]; '794 Patent, at [57]. These compositions facilitate delivery of a pharmaceutically active agent over varying gastrointestinal pH levels, particularly where the agent is pH dependent. The '794 patent specifies guanfacine as the pharmaceutically active agent. Col.3 ll.39-62. The claimed compositions comprise "at least one pharmaceutically active agent that is pH dependent, at least one non-pH dependent sustained release agent, and at least one pH dependent agent that increases the dissolution rate of the at least one pharmaceutically active agent at a pH in excess of 5.5." '599 Patent, at [57]; '794 Patent, at [57].

1. "*non-pH dependent sustained release agent*"

All the '599 patent claims, and claims 3, 6, 8, 11, and 12 of the '794 patent, claim a composition comprising, *inter alia*, a non-pH dependent sustained release agent. '599 Patent, col.7 l.33- col.10 l.16; '794 Patent, col. 15 l.6 - col. 16 l.39.

Plaintiffs' Proposed Construction	agent that slows release of the pharmaceutically active agent over an extended period of time regardless of gastrointestinal pH
Defendants' Proposed Construction	agent that slows the release of the pharmaceutically active agent in the gastrointestinal tract over an extended period of time regardless of the pH of the gastrointestinal tract, and that is not a pH-dependent agent
Court's Construction	agent that slows release of the pharmaceutically active agent over an extended period of time regardless of gastrointestinal pH, and that is not the pH-dependent agent

At argument, Defendants explained they were no longer proposing that the release be slowed "at substantially the same rate." (D.I. 198 at 58). Defendants also stated that their proposed pH modifier, "of the gastrointestinal tract," had the same meaning as Plaintiffs' proposed pH modifier, "gastrointestinal." *Id.* at 59-60. Plaintiffs' proposed modifier is more

accurate, as both patents disclose the composition functioning across gastrointestinal pHs outside the gastrointestinal tract, *in vitro* and in simulated gastric fluid. '599 and '794 patents, col.1 ll.24-27; '599 patent, col.4 ll.12-col.7 l.8; '794 patent, col.4 l.55-col.7 ll.3; col.7 ll.40-col.9 l.34.

The only substantive disagreement is therefore whether the non-pH dependent sustained release agent is mutually exclusive from the pH-dependent agent in the same composition; that is, whether one chemical can act as the non-pH dependent sustained release agent and the pH-dependent agent in the same composition. The parties submitted supplemental briefing on this issue in response to the Court's request at oral argument. (D.I. 204, 205). Plaintiffs argued and showed only that "an excipient can exhibit different properties in different formulations" "depending on context." (D.I. 204 at 1-2). Plaintiffs did not go so far as to argue that an excipient could exhibit different properties in the same formulation, as is necessary to support their proposed construction. Defendants argued that the two types of agents "must be separate and distinct agents for any given, static formulation." (D.I. 205 at 1). They did not argue that an excipient cannot act as one type of agent in one formulation, and a different type of agent in a different formulation.

The parties' positions do overlap: one excipient can act as different types of agents in different compositions or formulations, but cannot act as more than one type of agent in the same formulation. This is consistent with the patents' disclosure of specific excipients as both non-pH dependent sustained release agents and pH-dependent agents. *E.g.,* '599 Patent, col.1 l.63 and col.2 l.21 (listing carrageenan); *id.* col.1 l.63 and col.2 ll.8-11, 19-21 (listing sodium alginate). Neither proposed construction reflects this concurring position.

The term is construed to mean "agent that slows release of the pharmaceutically active agent over an extended period of time regardless of gastrointestinal pH, and that is not the pH-

dependent agent." The non-pH dependent sustained release agent cannot also be the pH-dependent agent in one single claimed composition, at the same time; as both parties pointed out, an excipient's role in a given formulation stems from its interactions with other excipients and/or the active agent in that formulation, as well as the excipient's concentration. (D.I. 204 at 1-2, D.I. 205 at 1). But there is no support for limiting an excipient from acting as a non-pH dependent sustained release agent in one composition and a pH-dependent agent in a different composition, particularly where the patents disclose the same excipients can act as both.

2. *"pH dependent agent that increases the rate of release of said at least one pharmaceutically active agent from the tablet at a pH in excess of 5.5"*

All the '599 patent claims, and claims 3 through 12 of the '794 patent, claim a composition comprising, *inter alia*, a pH dependent agent that increases the rate of release of the pharmaceutically active agent at a pH in excess of 5.5.[1] '599 Patent, col.7 l.33- col.10 l.16; '794 Patent, col. 15 l.6 - col. 16 l. 39.

Plaintiffs' Proposed Construction	agent that increases the rate of release of the pharmaceutically active agent from a tablet more in an environment that has a pH above 5.5 than in an environment that has a pH of 5.5 or below
Defendants' Proposed Construction	agent other than the pharmaceutically active agent, and that is not a non-pH dependent sustained release agent, and that is present in an amount sufficient to cause a statistically significant increase in the rate of release of the pharmaceutically active agent from a tablet more in the gastrointestinal tract in a pH above 5.5 than in the gastrointestinal tract in a pH of 5.5 or below
Court's Construction	agent that is neither the non-pH dependent sustained release agent nor the pharmaceutically active agent, and that increases the rate of release of the pharmaceutically active agent from a tablet more in an environment that has a pH above 5.5 than in an environment that has a pH of 5.5 or below.

[1] The '794 patent claims this agent as increasing the rate of release "from a tablet dosage form," while the '599 patent claims this agent as increasing the rate of release "from the tablet." The parties have not asserted that these differences require varying constructions, nor do varying constructions seem necessary.

Plaintiffs have requested the Court correct several alleged errors in the '599 and '794 patents, including the presence of the word "tablet" in this term, which Plaintiffs ask to be changed to "composition." (D.I. 199, 207). Defendants oppose Plaintiffs' request based on their interpretation of the standard for judicial correction set forth in *Novo Industries, L.P. v. Micro Molds Corp.*, 350 F.3d 1348, 1354 (Fed.Cir. 2003). (D.I. 203). Yet both parties have proposed constructions adopting the original term's use of "tablet," and neither party has asserted that an error within the term renders the term ambiguous and the claim indefinite.

The Court can, and will, construe the term as it appears. The Court will address the issue of error correction in the fuller context of invalidity arguments, on summary judgment or at trial. The word "tablet" in the Court's construction is subject to change to "composition" if the Court ultimately decides the term needs to be corrected, and the Court's decision to use "tablet" here does not prejudice any further argument as to whether the patent should be corrected (*i.e.*, at summary judgment on invalidity or at trial).

The parties dispute whether the agent must be present in an amount to cause a statistically significant increase in the rate of release, whether the applicable environment is the gastrointestinal tract, and whether the pH dependent agent can be a non-pH dependent sustained release agent. As explained in Section B1, *supra*, the patents disclose the claimed compositions *in vitro* and in simulated gastrointestinal fluid such that there is no support for limiting the claims to the gastrointestinal tract. 599 and '794 patents, col.1 ll.24-27; '599 patent, col.4 ll.12-col.7 l.8; '794 patent, col.4 l.55-col.7 ll.3; col.7 ll.40-col.9 l.34. This claim term already contains a pH limitation, making further limitation to the gastrointestinal pH range redundant.

As explained in Section B1, *supra*, the non-pH dependent sustained release agent cannot also be the pH-dependent agent in one claimed composition. Nor can the pH-dependent agent that increases the rate of release be the pharmaceutically active agent in the same composition;

the former acts on the latter, requiring a distinction between the two. The patents disclose three broad categories of pH-dependent agents: pH-dependent swelling polymers, enteric agents, and agents that increase the solubility of the pharmaceutically active agent. '599 and '794 Patents, col.2 ll.7-15. The patents do not disclose any overlap between those categories and the pharmaceutically active agent. *Compare id.* col. 1 ll.40-57 and *id.* col.2 ll.7-15. The pH dependent agent cannot be the non-pH dependent sustained release agent or the pharmaceutically active agent in the same composition.

Defendants argue that the limitation "present in an amount sufficient to cause a statistically significant increase in the rate of release" is necessary to ensure the agent caused an actual increase in the release rate, as opposed to an increase attributable to measuring error or some other cause. (D.I. 93 at 25-27). Defendants rely on the patents' reporting of standard deviations for dissolution data as support for their limitation requiring a statistically significant increase in release rate. *Id.* (citing '599 Patent, Table 2, col.5 ll.8-34; '794 Patent, Table 2, col.6 ll.41-67). Plaintiffs argue that these limitations are redundant, as the term and Plaintiffs' construction both require that the agent increase the rate of release. (D.I. 103 at 16); '599 Patent, col.7 ll.39-41. Plaintiffs argue that the patents' use of standard deviations to report dissolution data in a table should not be imported as a quantitative limitation on the increase of the rate of release, and note the patent does not quantitatively limit the increase of the rate of release in any other way. (D.I. 103 at 16-17; D.I. 198 at 80). Plaintiffs are correct: the term itself requires that the pH dependent agent actually increase the rate of release, and requiring that the increase be statistically significant is unsupported by the use of standard deviation in reporting dissolution data. The limitation "present in an amount sufficient to cause a statistically significant increase in the rate of release" is unwarranted.

This term is construed to mean "agent that is neither the non-pH dependent sustained release agent nor the pharmaceutically active agent, and that increases the rate of release of the pharmaceutically active agent from a tablet more in an environment that has a pH above 5.5 than in an environment that has a pH of 5.5 or below."

3. *"polymer that swells at a pH in excess of 5.5"*

The parties agree that this term is not at issue and need not be construed. (D.I. 226, 227).

4. *"enteric agent"*

Claims 3 and 10 of the '599 patent, and claims 6, 7, 11, and 12 of the '794 patent, claim a composition comprising a pH dependent agent where that agent is an "enteric agent." '599 Patent, col.7 l.45- col.8 l.42; '794 Patent, col. 15, l.38 - col. 16, l.39.

Plaintiffs' Proposed Construction	agent that resists dissolution or disruption in the stomach but not in the intestines
Defendants' Proposed Construction	agent that will not dissolve in the stomach, but will dissolve in the intestines, and that is not a non-pH dependent sustained release agent
Court's Construction	agent that resists dissolution in the stomach but not in the intestines

The patents define and claim "enteric agent" as a subcategory of pH dependent agents. '599 Patent, col.2 ll.8-12; *id.* col.7 ll.45-46; '794 Patent, col.2 ll.8-11; *id.* col. 15 ll.38-39. The limitation that the pH dependent agent "is not the non-pH dependent sustained release agent or the pharmaceutically active agent" therefore limits "enteric agent" as well. Defendants' proposed limitation that the enteric agent "is not a non-pH dependent sustained release agent" is rejected as redundant.

Defendants' proposed construction requires that the enteric agent be completely insoluble in the stomach, and relies primarily on extrinsic evidence. (D.I. 198 at 117-18, 120). But the patents themselves disclose some release of the active agent at gastric pH (1.2). '599 Patent,

col.4 l.9-col.5 l. 38; '794 Patent, col.4 l.53-col.7 l.3. Defendants' proposed limitation that the enteric agent not dissolve at all in the stomach is rejected for its inconsistency with this intrinsic evidence.

Plaintiffs' proposed construction is problematic in its use of the word "disruption." That word does not appear in either patent. (D.I. 198 at 84). The Court adopts Plaintiffs' proposed construction, less the unsupported phrase "or disruption." "Enteric agent" is construed to mean "agent that resists dissolution in the stomach but not in the intestines."

5. "*agent that increases the solubility of said at least one pharmaceutically active agent at a pH of greater than 5.5*"

Claims 4, 11, 12, and 14 of the '599 patent claim a composition including a pH dependent agent where that agent is an "agent that increases the solubility of said at least one pharmaceutically active agent at a pH of greater than 5.5." '599 Patent, col.7 l.47- col.8 l.56.

Plaintiffs' Proposed Construction	agent that increases the amount of the pharmaceutically active agent that will dissolve in a given amount of another substance to a greater extent in an environment which has a pH above 5.5 than in an environment which has a pH of 5.5 or below
Defendants' Proposed Construction	agent other than the pharmaceutically active agent, and that is not a non-pH dependent sustained release agent, and that is present in an amount sufficient to cause a statistically significant increase in the amount of the pharmaceutically active agent that will dissolve in a given amount of another substance, more in the gastrointestinal tract in a pH greater than 5.5 than in the gastrointestinal tract in a pH of 5.5 or below
Court's Construction	agent that increases the amount of the pharmaceutically active agent that will dissolve in a given amount of another substance to a greater extent in an environment which has a pH above 5.5 than in an environment which has a pH of 5.5 or below

The '599 Patent defines and claims agents that increase the solubility of the pharmaceutically active agent at a pH greater than 5.5 as a subcategory of pH dependent agents. Col.2, ll.8-15; *id.* col.7, ll.47-50. The limitation that the pH dependent agent "is not the non-pH dependent sustained release agent or the pharmaceutically active agent" therefore limits this

agent as well. Defendants' proposed limitation that this agent is "other than the pharmaceutically active agent, and that is not a non-pH dependent sustained release agent" is rejected as redundant. Defendants' proposed limitation that the agent be "present in an amount sufficient to cause a statistically significant increase," is rejected for the reasons set forth in Section B2, *supra*. Defendants' proposed limitation that the agent act "in the gastrointestinal tract" is rejected for the reasons set forth in Section B1, *supra*. This proposed limitation on pH is also redundant, as this term itself limits the agent's activity based on pH.

Therefore, the Court construes this term to mean "agent that increases the amount of the pharmaceutically active agent that will dissolve in a given amount of another substance to a greater extent in an environment which has a pH above 5.5 than in an environment which has a pH of 5.5 or below."

6. "*agent that maintains an acidic microenvironment in the composition*"

Claim 13 of the '599 patent claims a composition comprising a pH dependent agent where that agent is an "agent that maintains an acidic microenvironment in the composition." '599 Patent, col.8 ll.50-54.

Plaintiffs' Proposed Construction	agent that imparts an acidic character to the regions immediately around or in close proximity to the pharmaceutically active agent in the composition
Defendants' Proposed Construction	agent that is present in an amount sufficient to give the dissolving composition a pH of less than 5.5 in the regions immediately around or in close proximity to the pharmaceutically active agent in the composition and that is not a non-pH dependent sustained release agent
Court's Construction	agent that imparts an acidic character to the regions immediately around or in close proximity to the pharmaceutically active agent in the composition

The patent defines and claims agents that maintain acidic microenvironments as a subcategory of pH dependent agents. '599 Patent, col.2 ll.8-15; *id.* col.7 ll.50-54. The limitation that the pH dependent agent "is not the non-pH dependent sustained release agent or the

pharmaceutically active agent" therefore limits this agent as well. Defendants' proposed limitation that this agent is "not a non-pH dependent sustained release agent" is rejected as redundant. Defendants' proposed limitation that the agent be "present in an amount sufficient" to maintain the acidic microenvironment is rejected for the reasons set forth in Section B2, *supra*.

Defendants propose to limit "acidic microenvironment" to a pH of less than 5.5. The specification states these agents increase the solubility of the pharmaceutically active agent at a pH above 5.5. *Id.*, col.2 ll.28-29. This does not mean, however, that the acidic microenvironment the agent creates has a pH less than 5.5, particularly when the plain meaning of "acidic" is a pH of less than 7. (D.I. 103 at 21; D.I. 93 at 6). The Court adopts Plaintiffs' proposed construction.

7. "*reducing the likelihood of side effects associated with the administration of guanfacine*"

Claim 8 of the '794 patent claims a method of reducing the likelihood of side effects associated with the administration of guanfacine, comprising administration of a claimed guanfacine composition. Col.16 ll.4-24.

Plaintiffs' Proposed Construction	reducing the probability of side effects resulting from guanfacine administration
Defendants' Proposed Construction	decreasing the incidence of side effects compared to an immediate-release guanfacine formulation
Court's Construction	This term has a well understood meaning and does not require construction by the Court.

At oral argument, Plaintiffs noted that their proposed construction was at most the plain and ordinary meaning of the claim terms, and that the claim term was clear on its face and may not require construction. (D.I. 198 at 122-24). Defendants argue that "reduction of likelihood" requires a benchmark from which to measure, and that the specification's comparisons of the

side effects from the claimed formulation to those from an immediate release formulation provide that benchmark. *Id.* at 26; '794 Patent, col.11 l.61-col.13 l.67. Defendants argue that the incidence of side effects provides units by which to measure probability of side effects.

No construction of "reducing the probability of side effects resulting from guanfacine administration" is necessary; "reducing the probability" and "decreasing the incidence" are not appreciably different, and the latter does not assist one of skill in the art in understanding the claim term; and the Court declines to limit the term based on one example. *See Arlington Indus. v. Bridgeport Fittings, Inc.*, 632 F.3d 1246, 1252-56 (Fed.Cir. 2011); *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed.Cir.1997) (emphasizing that the claim construction process should not devolve into an "exercise of redundancy"); *e.g., Roche Diagnostics Operations, Inc. v. Abbott Diabetes Care*, 667 F.Supp.2d 429, 441-42 (D. Del. 2009).

The claim language shall be construed as set forth above.