UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF MICHIGAN
SOUTHERN DIVISION

ADAMS RESPIRATORY THERAPEUTICS, INC., ADAMS RESPIRATORY OPERATIONS, INC. AND ADAMS RESPIRATORY PRODUCTS, INC.,

Plaintiffs,

v. Case No. 1:07-CV-993

PERRIGO COMPANY, L. PERRIGO COMPANY AND PERRIGO RESEARCH AND DEVELOPMENT COMPANY, HON. GORDON J. QUIST

Defendants.
_____/

OPINION

Plaintiffs, Adams Respiratory Therapeutics, Inc., Adams Respiratory Operations, Inc., and Adams Respiratory Products, Inc. (collectively "Adams"), have sued Defendants, Perrigo Company, L. Perrigo Company, and Perrigo Research and Development Company (collectively "Perrigo"), alleging that Perrigo's proposed production and marketing of a generic version of Mucinex® will infringe Adams' patent, U.S. Patent No. 6,372,252 (the "'252 Patent"). The '252 Patent describes a sustained release formulation of guaifenesin and a modified release guaifenesin formulation consisting of an immediate release portion and a sustained release portion.

The Court has previously construed the disputed terms of the asserted claims of the '252 Patent. (Docket nos. 176, 187.) Perrigo has now moved for summary judgment of non-infringement, arguing that no reasonable jury could conclude that the accused product infringes the asserted claims of the '252 Patent as construed by the Court, either literally or under the doctrine

of equivalents. As part of its response to Perrigo's motion, Adams has filed a motion requesting that the Court reconsider its construction of the term "fully bioavailable in the subject's stomach."

For the reasons set forth below, the Court will deny Adams' motion for reconsideration and grant Perrigo's motion for summary judgment of non-infringement.

I. BACKGROUND AND PROCEDURAL HISTORY

Guaifenesin is an expectorant drug that has been used for many years in over-the-counter and prescription products to produce or "expectorate" phlegm from the bronchial airways to provide relief from coughs and congestion due to minor throat and bronchial irritations. The Food and Drug Administration ("FDA") first approved guaifenesin for use as an expectorant in 1952. For many years, drug manufacturers sold products containing guaifenesin, in both immediate and extended-release forms, without FDA approval. In 1989, FDA published Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Expectorant Drug Products for Over-the-Counter Human Use; Final Monograph; Final Rule ("Monograph"), in which FDA reviewed clinical trials relating to the use of an immediate release ("IR") form of guaifenesin as an expectorant and concluded that IR guaifenesin products would be deemed safe and effective, so long as they complied with the Monograph. *See* 54 Fed. Reg. 8494 (Feb. 28, 1989). Thus, a company seeking to market an IR guaifenesin product could do so without FDA approval if the product complied with the Monograph. However, because the Monograph did not address the safety and efficacy of extended-release guaifenesin products, it did not apply to the marketing or sale of those products. (Foster Responsive Report ¶ 10.)

On June 29, 2000, Adams submitted a New Drug Application ("NDA") pursuant to 21 U.S.C. §355(b) for approval of its extended-release guaifenesin product, Mucinex®. In lieu of requiring Adams to show that its extended release product was safe and effective, the FDA permitted

Adams to show that Mucinex® was "bioequivalent" to a standard IR dosage form of guaifenesin which complied with the Monograph. That is, Adams submitted pharmacokinetic (Pk) studies showing that Mucinex® has a C_{max}, or maximum concentration of guaifenesin in the blood, equivalent to Organidin, a standard immediate release product sold under the Monograph. In July of 2002, FDA approved 600 mg Mucinex® based upon its bioequivalence to a standard IR product. Shortly thereafter, FDA ordered all unapproved extended-release guaifenesin products off the market.

In April 2007, Perrigo filed an Abbreviated New Drug Application ("ANDA") seeking FDA approval to market a generic version of Adams' 600 mg Mucinex® product. Rather than comparing its ANDA product to a standard IR guaifenesin dosage under the Monograph, Perrigo sought to establish the safety and efficacy of its product by showing that it is bioequivalent to Mucinex®. In other words, Perrigo relied solely upon Pk studies showing, among other things, that the C_{max} of its ANDA product is bioequivalent to Mucinex®. Because Adams had listed the '252 Patent in the "Orange Book" as covering Mucinex®, Perrigo also filed a "paragraph IV" certification asserting that the '252 Patent is invalid or would not be infringed by Perrigo's generic drug. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV). Perrigo also notified Adams of its paragraph IV certification. In response, Adams filed the instant patent infringement suit under 35 U.S.C. § 271(e)(2)(A) on the basis of Perrigo's ANDA filing.

On July 24, 2009, the Court issued an Order providing the parties its "Proposed Construction of Disputed Terms" of the asserted claims, being claims 24, 26, 33, 34, and 39 of the '252 Patent. Pursuant to that Order, the parties filed additional briefs, and the Court held a *Markman* hearing on August 21, 2009. On August 24, 2009, the Court issued an Order adopting its proposed claim construction. Of particular relevance to the instant motions, the Court construed the following terms

found in claim 24, from which all other asserted claims depend: (1) "equivalent" means "within 80% to 125% of the value which is being compared, at a 90% confidence interval" (docket no. 176 at 35-36); and (2) "fully bioavailable in the subject's stomach" means "the active pharmaceutical ingredient is thoroughly absorbed in the subject's stomach" (*id.* at 28-31).

II. DISCUSSION

Perrigo contends that it is entitled to summary judgment of non-infringement because Adams cannot show that Perrigo's ANDA product meets two limitations applicable to all asserted claims. In particular, Perrigo argues that Adams has no evidence that the accused product:

(1) "provides a C_{max} in a human subject equivalent to the C_{max} obtained when the first of three doses of a standard immediate release formulation having one third the amount of guaifenesin is dosed every four hours over a 12 hour period"; and

(2) contains a first portion that "comprises a first quantity of guaifenesin in an immediate release form which becomes fully bioavailable in the subject's stomach."

Perrigo further contends that Adams has no evidence that it infringes claim 34 because Adams cannot show that Perrigo's ANDA product "has an AUC_{inf} of at least 3500 hr*ng/mL."

Adams responds that it has sufficient evidence to show that Perrigo's ANDA product meets these claim limitations. In addition, Adams requests that the Court reconsider its construction of the term "an immediate release form which becomes fully bioavailable in the subject's stomach" because under the Court's construction the claims literally do not cover the preferred embodiment of the '252 Patent.

A. Adams' Motion for Reconsideration

To prevail on a motion for reconsideration, the movant must "not only demonstrate a palpable defect by which the Court and the parties have been mislead, but [must] also show that a

different disposition of the case must result from a correction thereof." *See* LCivR 7.4(a). A motion for reconsideration may not be used to simply rehash rejected arguments or to introduce new arguments. *See Westbrook v. Comm'r*, 68 F.3d 868, 879 (5th Cir. 1995).

Adams argues that the Court should reconsider its construction of the term "an immediate release form which becomes fully bioavailable in the subject's stomach" as "the active pharmaceutical ingredient is thoroughly absorbed in the subject's stomach." Instead, it contends, the Court should adopt the construction proposed by its expert, Dr. Foster, which is "a dosage form that releases substantially all of the drug particles relatively quickly upon ingestion (*i.e.* in the stomach)." Adams contends that reconsideration is required because Perrigo's experts now admit that the claims, as this Court has construed them, do not literally cover the preferred embodiment, *i.e.*, Mucinex®, because: (1) it is generally understood in the pharmaceutical field that the small intestine is the primary site for absorption of all drugs with little, if any, drug absorption occurring in the stomach; and (2) no measurable amount of any guaifenesin formulation, including the preferred embodiment, is absorbed through the stomach. Adams contends that reconsideration is warranted because a construction which excludes the preferred embodiment, such as the Court's construction does in this case, is improper under Federal Circuit law.[1]

As Adams correctly notes, the Federal Circuit has held that a claim construction that excludes the preferred embodiment "is rarely, if ever correct and would require highly persuasive evidentiary support . . . ." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996). Nevertheless, this statement cannot be construed as a categorical rule against a construction that excludes the preferred embodiment. As the Federal Circuit has observed, "where we conclude

[1]Adams' motion for reconsideration is authorized by this district's local rules, and a court retains the authority to reconsider prior claim construction rulings where appropriate. *See Dexas Int'l, Ltd. v. Office Max Inc.*, No. 6:07cv396, 2009 WL 252164, at *10 (E.D. Tex. Jan. 30, 2009).

that the claim language is unambiguous, we have construed the claims to exclude all disclosed embodiments." *Lucent Techs., Inc. v. Gateway, Inc.*, 525 F.3d 1200, 1215-16 (Fed. Cir. 2008). This is because the principal Adams cites generally applies when a claim "term has multiple ordinary meanings consistent with the intrinsic record." *Helmsderfer v. Bobrick Washroom Equip., Inc.*, 527 F.3d 1379, 1383 (Fed. Cir. 2008). In such cases, a court must adopt the construction that aligns with the preferred embodiment. On the other hand, where the claim language is unambiguous and admits of only one meaning, a court must so construe the claim, even where the construction excludes the preferred embodiment, because "[c]ourts cannot rewrite claim language." *Id.*

In construing the phrase "fully bioavailable in the subject's stomach,"the Court looked to the ordinary meaning of the term "bioavailable" within the art as referring to absorption rather than release of the drug. Specifically, the Court noted that the term "bioavailable" has a well-known meaning in the sciences of medicine and pharmacology pertaining to absorption. (Docket no. 176 at 28.) Adams contends that the Court's erroneous construction resulted from its consideration of extrinsic evidence (Perrigo's expert's claim construction declaration) "that has proven misleading and contrary to scientific principles." (Pls'. Br. Supp. Mot. Recons. at 9.) While it is true that the Court relied on extrinsic evidence, including the *Merck Manual of Diagnosis and Therapy* as well as the Code of Federal Regulations, the Court also considered the intrinsic evidence, including the claim language, the specification, and the file history, and concluded that the term "bioavailable" was intended to have its ordinary meaning. For example, in its Claim Construction, the Court noted that the specification recognized the distinction between release and absorption by stating that "'quick[] release [of] the guaifenesin . . . results in rapid bioavailablity.'" (Docket no. 176 at 29, quoting '252 Patent, Col. 1, ll. 50-52.) Similarly, at the final pretrial conference held on December 15, 2009, the Court cited other language in the specification recognizing the distinction between

dissolution and absorption, or bioavailability. (12/15/09 Hr'g Tr. at 16-20 (citing Col. 2, ll. 50-52 ("Furthermore, every medicament has different solubility properties and pH dependencies which affect its dissolution rate, *and hence* bioavailability" (italics added).) Nothing Adams offers in support of its motion suggests that the term "bioavailable" had a meaning other than that which the Court adopted.

Adams further argues:

> Contrary to what Perrigo and Dr. Chambliss told the Court during claim construction, one of ordinary skill in the art could not understand the claims to require 100% absorption, or even "thorough" absorption, in the stomach. This is true because to so construe the claims, a person of ordinary skill in the art would have to ignore the fact that the intestine is the main site of drug absorption and conclude that the inventors intended, for some inexplicable and self-defeating reason, to define the scope of their invention so as to literally exclude any guaifenesin formulation, including the preferred embodiment expressly described in the '252 patent, which would be inconsistent with scientific principles.

(Pls.' Br. Supp. Mot. Recons. at 8.) In other words, why would the inventors do such a thing? The same question was probably raised by the patentee in *Chef America, Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371 (Fed. Cir. 2004), in which the claimed invention was a process for precooking a dough product that would have a light, flaky texture upon final cooking at a later time. The claim at issue required "heating the resulting batter-coated dough to a temperature in the range of about 400˚ F. to 850˚." *Id.* at 1373. The court observed that literal application of this claim language, consisting of "ordinary, simple English words whose meaning is clear and unquestionable," would produce a dough product "burned to a crisp" and "resembl[ing] a charcoal briquet" – something the inventor would never have intended. *Id.* Applying the oft-repeated rule that "courts may not redraft claims, whether to make them operable or to sustain their validity," the court held that it was compelled to "construe the claim as written, not as the patentees wish they had written it." *Id.* at 1374.

So, why would the inventors of the '252 Patent define their invention by saying that the guaifenesin is fully bioavailable, i.e., absorbed, in the stomach? This Court can only speculate. Only the inventors and their lawyers who prosecuted the patent application know the answer. Regardless, in construing this language, the Court considered all available evidence – both intrinsic and extrinsic – and concluded that "bioavailable" has a well-recognized meaning that always refers to absorption into the body. Adams has still not offered any evidence to the contrary. As the Federal Circuit stated in *Chef America*, courts may not redraft a claim that is subject to only one reasonable interpretation, even if the construction is "nonsensical." *Id.* at 1374. Because the term "bioavailable" has a meaning that is well known in the art, the Court concludes that it did not err in construing that term as referring to absorption rather than release or dissolution.

B. Perrigo's Motion for Summary Judgment

Summary judgment is appropriate if there is no genuine issue as to any material fact and the moving party is entitled to a judgment as a matter of law. Fed. R. Civ. P. 56. Material facts are facts which are defined by substantive law and are necessary to apply the law. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248, 106 S. Ct. 2505, 2510 (1986). A dispute is genuine if a reasonable jury could return judgment for the non-moving party. *Id.*

The court must draw all inferences in a light most favorable to the non-moving party, but may grant summary judgment when "the record taken as a whole could not lead a rational trier of fact to find for the non-moving party." *Agristor Fin. Corp. v. Van Sickle*, 967 F.2d 233, 236 (6th Cir. 1992) (quoting *Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 587, 106 S. Ct. 1348, 1356 (1986)).

"An infringement analysis entails two steps. The first step is determining the meaning and scope of the patent claims asserted to be infringed. The second step is comparing the properly

construed claims to the device accused of infringing." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc) (citations omitted). Because the Court has already construed the disputed claim terms, to determine infringement it need only compare Perrigo's ANDA product to the asserted claims. In order "to find infringement, the accused device must contain 'each limitation of the claim, either literally or by an equivalent.'" *TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc.*, 529 F.3d 1364, 1379 (Fed. Cir. 2008) (quoting *Freedman Seating Co. v. Am. Seating Co.*, 420 F.3d 1350, 1358 (Fed. Cir. 2005)). "If . . . even one claim is missing or not met, there is no literal infringement." *MicroStrategy Inc. v. Bus. Objects, S.A.*, 429 F.3d 1344, 1352 (Fed. Cir. 2005). The patentee, in this case Adams, bears the burden of proving infringement by a preponderance of the evidence. *Ultra-Tex Surfaces, Inc. v. Hill Bros. Chem. Co.*, 204 F.3d 1360, 1364 (Fed. Cir. 2000).

1. C_{max} Equivalent to the C_{max} of a Standard Immediate Release Formulation

Perrigo contends that it is entitled to summary judgment because Adams can offer no evidence showing that Perrigo's ANDA product "provides a C_{max} in a human subject equivalent to the C_{max} obtained when the first of three doses of a standard immediate release formulation having one third the amount of guaifenesin is dosed every four hours over a 12 hour period." ('252 Patent, Col. 22, ll. 23-27.) Perrigo points out that Adams' only argument on this claim limitation is that Perrigo literally infringes because its ANDA product has a mean C_{max} that is equivalent to Mucinex® and is therefore equivalent to a standard IR guaifenesin product. In other words, Perrigo argues, Adams attempts to show that Perrigo's ANDA product meets this claim limitation solely by comparing Perrigo's product with Mucinex®. Perrigo argues that Adams cannot prove infringement in this manner because it is legally impermissible for a court to conduct an infringement analysis

by comparing the accused product to the patentee's commercial embodiment. Rather, Perrigo argues, Adams must compare the accused product directly with the claims of the '252 Patent, but it lacks the evidence to do so.

Adams responds that it has "pointed to a wealth of affirmative evidence that [Perrigo's] ANDA product does have a C_{max} equivalent to a standard immediate release product." (Pls.' Mem. Opp'n Defs.' Mot. at 9.) Adams argues that Perrigo essentially used Mucinex® as a proxy for a standard IR product in representing to the FDA that its ANDA product is safe and effective because it is bioequivalent to Mucinex®. Thus, Adams argues, there is no reason why it should not be able to rely on a comparison of Perrigo's ANDA product to Mucinex® in order to show that Perrigo's ANDA product has a C_{max} equivalent to an IR product and, therefore, meets this limitation. Adams further argues that the claims do not require a head-to-head cross-over study and the Court should not read such a limitation into the claims. Finally, Adams contends that the Federal Circuit has not imposed a blanket prohibition against comparing the commercial embodiment to the accused product as "part of" an infringement analysis.

The scope of a court's infringement analysis is well defined:

> [T]he law of infringement compares the accused product with the claims as construed by the court. Infringement, either literally or under the doctrine of equivalents, does not arise by comparing the accused product "with a preferred embodiment described in the specification, or with a commercialized embodiment of the patentee."

Johnson & Johnson Assocs. Inc. v. R.E. Serv. Co., 285 F.3d 1046, 1052 (Fed. Cir. 2002) (quoting *SRI Int'l v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1121 (Fed. Cir. 2002)). *See also Spectrum Int'l, Inc. v. Sterilite Corp.*, 164 F.3d 1372, 1381 (Fed. Cir. 1998) ("To be sure, a court may not predicate an infringement determination on a comparison of an accused product with a patentee's commercial embodiment."); *Zenith Labs. v. Bristol-Meyers Squibb Co.*, 19 F.3d 1418, 1423 (Fed. Cir. 1994)

("As we have repeatedly said, it is error for a court to compare in its infringement analysis the accused product or process with the patentee's commercial embodiment or other version of the product or process; the only proper comparison is with the claims of the patent."). Adams has not cited any case in which the Federal Circuit has held that a different framework applies in ANDA cases. In fact, courts have, not surprisingly, applied these same rules in such cases. *See Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003) (stating that "the substantive determination whether actual infringement or inducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits, including those in a non-ANDA context"); *Wyeth v. Mylan Pharms., Inc.*, No. 1:07CV91, 2009 WL 3335062, at * 3 (N.D.W. Va. Oct. 14, 2009) ("[T]he Court . . . must compare Mylan's proposed generic version of Effexor® XR to th[e] claims. Importantly, it must compare Mylan's proposed product to the asserted method claims of the patents in suit rather than to Effexor XR®.") (citing *Zenith Labs*); *Abbott Labs. v. TorPharm, Inc.*, No. 97 C 7515, 2003 WL 22462614, at *22-23 (N.D. Ill. Oct. 29, 2003) (following *Zenith* and holding that Federal Circuit law precludes a party from establishing infringement by comparing the accused product to the patentee's commercial embodiment). Likewise, in cases such as this, the patentee retains the burden of presenting evidence to show that the proposed product will infringe the asserted patent claims. *Warner-Lambert*, 316 F.3d at 1366. Thus, Adams' assertions that Perrigo's motion must be denied because Perrigo "cite[s] ***no*** evidence that the C_{max} of its proposed ANDA product is ***not*** equivalent to the C_{max} of a standard immediate release product," and "there is no evidence that the product disclosed in [Perrigo's] ANDA always (or even usually) avoids the C_{max} claim limitation," (Pls.' Mem. Opp'n Defs.' Mot. at 8), offer no basis for denying Perrigo's motion. Rather, Adams must offer affirmative evidence of infringement.

As Adams readily admits, its sole infringement evidence with respect to the C_{max} claim limitation is based upon a comparison of Perrigo's ANDA product to Mucinex®, Adams' commercial embodiment. Adams' expert, Dr. Foster, explains: "Perrigo literally infringes this claim element because its ANDA product has a mean C_{max} that is equivalent to Mucinex®, and thus equivalent to a standard immediate-release product, such as Organidin® NR." (Foster 8/10/09 Report ¶ 78.) Stated differently, Adams argues that if A is equivalent to B, and B is equivalent to C, then A must be equivalent to C. But, as set forth above, this type of analysis is improper. Instead, Adams must present evidence directly comparing the accused product to the claims of the patent, i.e., it must show that Perrigo's ANDA product has a C_{max} equivalent to a standard IR product. Adams has not presented such evidence, and it admits that it has none. (*Id.* ¶ 79.) Because Adams' comparison of the accused product to its preferred embodiment is legally impermissible, Adams has failed to meet its burden of presenting admissible evidence to create a genuine issue of material fact on its infringement claim.

Adams cites a number of cases as supporting its assertion that "[t]here is no blanket prohibition against considering evidence concerning the patentee's commercial embodiment as part of an infringement inquiry." (Pls.' Mem. Opp'n Defs.' Mot. at 13.) None of those cases holds that it is permissible for a patentee to prove infringement without comparing the accused product to the asserted claims, as Adams seeks to do. For example, in *Glaxo Group Ltd. v. TorPharm, Inc.*, 153 F.3d 1366 (Fed. Cir. 1998), the court distinguished the facts of the case from those in *Zenith*, *supra*, upon the ground that Glaxo's expert showed that the calibrated sample included all 29 main peaks and therefore met all of the claim limitations. *Id.* at 1373. However, the court did not disavow *Zenith's* admonition against comparing the accused device to the commercial embodiment.

Moreover, even if Adams were legally permitted to prove infringement by comparing Perrigo's ANDA product with Mucinex®, Perrigo has shown why Adams cannot prove through this comparison that Perrigo's ANDA product has a C_{max} equivalent to a standard IR product.

The Court construed "equivalent" in accordance with FDA's bioequivalence definition – within 80% to 125% of the value which is being compared, at a 90% confidence interval. To show bioequivalence, FDA requires an applicant to submit evidence comparing the propose drug to the approved drug or "reference drug." *See* 21 U.S.C. § 355(j)(2)(A)(iv); 21 C.F.R. § 320.21(b)(1). The standard method for proving bioequivalence is a two-treatment crossover study on a group usually consisting of between 24 and 36 volunteers. *See* FDA *Approved Drug Products with Therapeutic Equivalence Evaluations* at viii (29th ed. 2009). Single doses of the test drugs are administered to the subjects and blood and plasma levels of the test subjects are measured over time. *Id.* The log-transformed mean of the particular parameter (C_{max} or AUC) is calculated from the results for each product, and a ratio between the two means is obtained. *Id.* at ix. Finally, a 90% confidence interval is calculated around that ratio. If the confidence interval is within 80% to 125%, then the FDA considers the proposed product bioequivalent to the reference drug. *Id.* Because a two-way crossover study is required to prove bioequivalency, a direct comparison between the two drugs is required. (Chambliss Responsive Report ¶ 115.) Dr. Bolton, one of Perrigo's experts, explains why Adams' indirect comparison is unreliable:

> There are numerous reasons why [a] comparison of B to A; B to C; C to A cannot be made to assess whether Perrigo R&D's ANDA product is equivalent to a standard immediate release product, under the Court's construction. One example is the fact that determining whether two products are equivalent requires the calculation of a *confidence interval* and one cannot properly calculate the confidence interval necessary to determine equivalence with a comparison of this kind. That is to say, the confidence interval needed to determine whether two products are equivalent is not acceptable using the mean C_{max} from an entirely different study. The FDA guidance for determining bioequivalence for these products requires a cross-over

> study where each individual takes each product on two occasions. Thus, the proper comparison is within-individual comparison, rather than a comparison between products taken by different individuals. . . . . Again, the declaration that two products are equivalent can only be made based on the results and analysis of a head to head cross-over study.

(Bolton 9/14/09 Report ¶ 20; see also Foster Dep. at 40-41 ("a bioequivalent study by its very definition requires minimally and ideally a crossover design where the subject is crossed over from the test product to the reference product").) In addition, as Perrigo notes, an FDA administrative ruling involving the branded drug Effexor XR capsules reinforces the conclusion that Adams cannot demonstrate bioequivalence between Perrigo's ANDA product and a standard IR formulation by showing that Perrigo's ANDA product is bioequivalent to Mucinex®. (11/25/08 FDA Administrative Ruling, Docket No. FDA-2008-P-0329.) Furthermore, the Federal Circuit has explained that bioequivalence and patent infringement by equivalents are distinct concepts and serve different purposes:

> [B]ioequivalency and equivalent infringement are different inquiries. Bioequivalency is a regulatory and medical concern aimed at establishing that two compounds are effectively the same for pharmaceutical purposes. In contrast, equivalency for purposes of patent infringement requires an element-by-element comparison of the patent claim and the accused product, requiring not only equivalent function but also equivalent way and result. Different attributes of a given product may thus be relevant to bioequivalency but not equivalent infringement, and vice versa. . . . . Thus, while potentially relevant, the bioequivalency of an accused product with a product produced from the patent at issue is not sufficient to establish infringement by equivalents.

Abbott Labs. v. Sandoz, Inc., 566 F.3d 1282, 1298 (Fed. Cir. 2009). Accordingly, the basis for Adams' claim that Perrigo's ANDA product has a C_{max} equivalent to a standard IR product must be rejected.

Finally, Adams contends requiring a direct study comparing Perrigo's ANDA product to a standard IR product would be improper because the claims require no such study and imposing such

a requirement would read a limitation into the claim. The Court disagrees. A two-way crossover study is simply the scientific means for determining whether two products have an equivalent C_{max}. As noted above, a crossover study is a generally recognized means of determining bioequivalence. Therefore, Adams' infringement claim fails both literally and under the doctrine of equivalents. *See Johnson & Johnson Assocs.*, 285 F.3d at 1052.

2. Fully Bioavailable in the Subject's Stomach

Perrigo further contends that Adams cannot prove its infringement claim for the additional reason that Adams has no evidence that Perrigo's ANDA product has "a first portion compris[ing] a first quantity of guaifenesin in an immediate release form which becomes fully bioavailable in the subject's stomach." As noted above, the Court construed "fully bioavailable in the subject's stomach" to mean "the active pharmaceutical ingredient is thoroughly absorbed in the subject's stomach." Perrigo contends that Adams has no evidence showing that this limitation is met, either literally or by the doctrine of equivalents, because there is no evidence that any guaifenesin is thoroughly absorbed in the stomach. The Court agrees.

In support of its argument Perrigo cites the opinions of its experts, Drs. Chambliss and Mayersohn, both of whom state that drug absorption generally occurs in the intestines rather than the stomach. In his responsive report, Dr. Chambliss notes that Adams' expert, Dr. Amidon, has published extensively on the subjects of gastric emptying time and drug absorption and that "Dr. Amidon's publications contain many statements that support the concept that, generally, drug absorption occurs mainly in the intestines, not the stomach." (Chambliss Responsive Report ¶¶ 95-96.) Dr. Chambliss cites several publications by Dr. Amidon that support his own opinion that guaifenesin is absorbed in the small intestine rather than the stomach. (*Id.* ¶¶ 96-101.) In addition, Dr. Chambliss notes that in spite of his extensive knowledge and experience on the subject, Dr.

Amidon does not opine on whether guaifenesin is thoroughly absorbed in the stomach. (*Id.* ¶ 94.) Dr. Mayersohn similarly concludes that drug absorption occurs in the small intestine rather than the stomach because after the drug is released from the tablet and dissolved in the gastrointestinal fluids, it would not remain in the stomach for any length "but fairly quickly empties into the small intestine." (Mayersohn Rebuttal Report ¶ 24.) Dr. Mayersohn, like Dr. Chambliss, cites a number of publications, including several authored by Dr. Amidon, showing that very little, if any, drug absorption occurs in the stomach.

In contrast, Adams' only support for Perrigo's ANDA product having a quantity of guaifenesin that is thoroughly absorbed in the stomach comes from Dr. Foster. Dr. Foster asserts that Perrigo's "tablet would be in the stomach for about 2 hours"; that Pk data from a standard IR guaifenesin product shows that the peak plasma concentration (T_{max}) occurs at about 1.70-2.0 hours following dosing; the Pk profile of a Mucinex® and a standard IR product shows that they have "essentially the same" C_{max} and T_{max}; Perrigo's Pk data shows that its ANDA product "has the same C_{max} and T_{max} as Mucinex®"; and "[t]hus, the immediate release portion of Perrigo's tablet dissolves at about the same rate and in much the same way as Mucinex® and it therefore is thoroughly absorbed from the stomach." (Foster 8/10/09 Report ¶¶ 54-56.) Dr. Foster adds that "at 2 hours, 38.97% of the Perrigo's ANDA product has already been absorbed." (*Id.* ¶ 58.) As Perrigo notes, however, Dr. Foster's opinion is based solely upon conjecture. That is, while the evidence upon which Dr. Foster relies shows the length of time the tablet remains in the stomach and when and how much of the guaifenesin is released into the stomach and absorbed by the body, it does not show where the absorption occurs. Adams, itself, recognizes in its response that Dr. Foster's assertions are insufficient to prove that guaifenesin is thoroughly absorbed in the stomach by conceding that it cannot prove literal infringement.

Although conceding literal infringement, Adams argues that Perrigo's ANDA product infringes under the doctrine of equivalents. "An accused device that does not literally infringe a claim may still infringe under the doctrine of equivalents if each limitation of the claim is met in the accused device either literally or equivalently." *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1459 (Fed. Cir. 1998) (en banc). Infringement under this doctrine requires that any difference between the claim elements at issue and the corresponding elements of the accused product be insubstantial. *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 39-40, 117 S. Ct. 1040, 1054 (1997).

Adams contends that it can prove infringement by equivalents because its experts, Drs. Foster and Amidon believe that it is irrelevant or insignificant where absorption occurs. Dr. Foster states:

> Ultimately, I believe that it is insignificant whether guaifenesin is absorbed entirely from the stomach, or whether guaifenesin is absorbed in the stomach as well as the remainder of the gastrointestinal tract. Either way, the same function and result occurs: the guaifenesin in the IR portion of Perrigo's ANDA tablet is rapidly absorbed into the bloodstream, regardless of where in the gastrointestinal tract absorption occurs. . . .

(Foster Rebuttal Report ¶ 29.) Similarly, Dr. Amidon states:

> In my view, whether the guaifenesin in the IR portion of Perrigo's product is actually absorbed through the stomach mucosa or the small intestine (or elsewhere in the GI tract) is not important to the function of the product or the IR portion. In either case, the IR portion of Perrigo's product is still performing substantially the same function in substantially the same way to achieve the same result.

(Amidon Rebuttal Report ¶ 92.)

Even assuming that the site of absorption is not significant, the "all elements" rule precludes Adams from establishing infringement under the doctrine of equivalents. The "all elements" rule provides that "an accused product or process is not infringing unless it contains each limitation of

the claim, either literally or by an equivalent." *Freedman Seating Co. v. Am. Seating Co.*, 420 F.3d 1350, 1358 (Fed. Cir. 2005) (citing *Warner-Jenkinson Co.*, 520 U.S. at 29, 117 S. Ct. at 1054). "[A]n element of an accused product or process is not, as a matter of law, equivalent to a limitation of the claimed invention if such a finding would entirely vitiate the limitation." *Id.* (citing *Warner-Jenkinson Co.*, 520 U.S. at 29, 117 S. Ct. at 1054). In determining whether a finding of infringement under the doctrine of equivalents would vitiate a claim limitation, a court must consider the totality of the circumstances, including "whether the alleged equivalent can be fairly characterized as an insubstantial change from the claimed subject matter without rendering the pertinent limitation meaningless." *Id.* at 1359.

In *Novartis Pharmaceuticals Corp. v. Eon Labs Manufacturing, Inc.*, 363 F.3d 1306 (Fed. Cir. 2004), the patent at issue covered a formulation for administering cyclosporin as a hydrosol. The patentee argued that the term "hydrosol" should be "broadly defined to include a dispersion of solid particles in aqueous colloidal solution formed in a patient's stomach." *Id.* at 1309-10. The Federal Circuit concluded that the term should be construed more narrowly, as "limited to medicinal preparation consisting of a dispersion of solid particles in a liquid colloidal solution prepared outside the body." *Id.* at 1311. The court then concluded that there was no literal infringement because the accused product took the form of a hydrosol only after ingestion. *Id.* at 1312. The court further found that the accused product did not infringe under the doctrine of equivalents:

> Here the formation of a particulate dispersion inside the body cannot infringe under the doctrine of equivalents because this would vitiate the claimed requirement that the dispersion be prepared outside the body. Infringement under the doctrine of equivalents requires that any difference between the claim elements at issue and the corresponding elements of the accused product be insubstantial. To extend the scope of the claims at issue to encompass a dispersion formed inside the stomach would necessarily read the "hydrosol" limitation out of those claims.

Id. (citation omitted).

The Court finds the reasoning in *Novartis* applicable to the claims in this case because a finding of infringement based upon absorption at a site other than the stomach would entirely vitiate the "fully bioavailable in the subject's stomach" limitation from the claim. The place of absorption is not insubstantial. In fact, the meaning of this claim language was a point of substantial contention during claim construction, with Adams arguing that the drug had to release fairly quickly upon ingestion and Perrigo arguing that absorption had to occur entirely in the subject's stomach. Ultimately the Court construed the term to mean that the drug is "thoroughly absorbed in the subject's stomach." To allow Adams to ignore this limitation would impermissibly expand the scope of the claim as determined by the Court. Thus, Perrigo's ANDA product also lacks this claim limitation.

3. An AUC_{inv} of at Least 3500 hr*ng/mL

Perrigo also argues that it is entitled to summary judgment on this limitation in claim 34. Because the Court has already concluded that Adams's infringement claim fails because Perrigo's ANDA products lacks the limitations discussed above, the Court need not address this argument. However, because the argument requires little analysis, the Court will address it.

Perrigo contends that its ANDA product does not infringe claim 34, either literally or under the doctrine of equivalents, because its product does not have "an AUC_{inf} of at least 3500 hr*ng/mL." Perrigo's product has four mean AUC_{inf} values, none of which is "at least 3500." The term "at least" means "'as the minimum,' and therefore when coupled with a specific number sets forth an absolute lower limit of a range, i.e., 600 on up." *Quantum Corp. v. Rodime, PLC*, 65 F.3d 1577, 1581 (Fed. Cir. 1995) (quoting *Webster's Third New International Dictionary* 1287 (1986)). Because this limitation sets forth a minimum value of 3500, Perrigo's product does not literally infringe. Moreover, the Court concludes that Perrigo is entitled to summary judgment on this claim

under the doctrine of equivalents because allowing Adams to claim a value below "at least 3500" would improperly vitiate this claim limitation. *See Novartis*, 363 F.3d at 1312.

III. CONCLUSION

For the foregoing reasons, the Court will deny Adams' motion for reconsideration and grant Perrigo's motion for summary judgment of non-infringement.

An Order consistent with this Opinion will be entered.

Dated: February 11, 2010

/s/ Gordon J. Quist
GORDON J. QUIST
UNITED STATES DISTRICT JUDGE